

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:46:31 ON 02 FEB 2003  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
jan.delaval@uspto.gov

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 2 Feb 2003 VOL 138 ISS 6  
FILE LAST UPDATED: 31 Jan 2003 (20030131/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 13:21:49 ON 02 FEB 2003)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:21:59 ON 02 FEB 2003

E GDF/CN  
L1 1 S E31  
L2 2 S E32-E34  
E GROWTH DIFFERENTIATION FACTOR/CN  
L3 1 S E16  
L4 1 S L1,L3

FILE 'HCAPLUS' ENTERED AT 13:23:04 ON 02 FEB 2003

L5 47 S L4  
L6 149 S MYOSTATIN  
L7 96 S (GDF OR GROWTH DIFFERENTIAT? FACTOR) (S) 8  
L8 199 S L5-L7  
E KLYSNER S/AU  
L9 8 S E3,E4  
E MOURITSEN S/AU  
L10 44 S E3-E5  
E HALKLER T/AU  
E HALKIER T/AU  
L11 73 S E3,E4  
L12 2 S L8 AND L9-L11

FILE 'REGISTRY' ENTERED AT 13:26:28 ON 02 FEB 2003

E MYOSTATIN  
L13 179 S E3

FILE 'HCAPLUS' ENTERED AT 13:26:41 ON 02 FEB 2003

L14 74 S L13  
L15 201 S L8,L14

FILE 'REGISTRY' ENTERED AT 13:27:17 ON 02 FEB 2003

L16 185 S (GROWTH(L) DIFFERENTIAT?(L) FACTOR(L) 8)/INS.HP

FILE 'HCAPLUS' ENTERED AT 13:27:56 ON 02 FEB 2003

L17 65 S L16  
 L18 203 S L15,L17  
 L19 2 S L9-L11 AND L18  
 L20 1 S L19 AND DOWN REGULAT?  
 SEL RN

FILE 'REGISTRY' ENTERED AT 13:29:02 ON 02 FEB 2003

L21 44 S E1-E44  
 L22 22 S L21 AND L1-L4,L13,L16  
 L23 22 S L21 NOT L22  
 L24 13 S L23 AND SQL/FA  
 L25 9 S L23 NOT L24

FILE 'HCAPLUS' ENTERED AT 13:29:59 ON 02 FEB 2003

L26 62 S L24  
 L27 5 S L26 AND L9-L11  
 L28 5 S L20,L27  
 L29 13 S L18 AND (DOWNREGULAT? OR DOWN REGULAT?)  
 L30 5 S L18 AND (VACCIN? OR IMMUNIZ? OR IMMUNIS?)  
 L31 11 S L18 AND INJECT?  
 L32 84 S L18 AND (MUTAT? OR INSERT? OR DELET? OR ADDITION? OR SUBSTITU  
 L33 9 S L18 AND CHIMER?  
 L34 10 S L29-L31 AND L32,L33  
 L35 31 S L29-L31,L20,L28,L34  
 L36 18 S L18 AND RECOMBIN?  
 L37 46 S L35,L36  
 L38 46 S L37 AND L5-L12,L14,L15,L17-L20,L26-L37  
 L39 17 S L38 AND (PD<=19990726 OR PRY<=19990726 OR AD<=19990726)  
 L40 18 S L28,L39  
 SEL DN AN 1 2 10 12 14 16 17 18  
 L41 10 S L40 NOT E45-E68  
 L42 8 S L40 NOT L41  
 SEL DN AN 4  
 L43 1 S L42 AND E69-E71  
 L44 11 S L41,L43  
 E MUTATION/CT  
 L45 25 S E3-E42 AND L18  
 E E3+ALL  
 L46 25 S E1+NT AND L18  
 L47 25 S L45,L46  
 L48 16 S L47 AND (PD<=19990726 OR PRY<=19990726 OR AD<=19990726)  
 L49 14 S L48 NOT L40  
 L50 11 S L49 AND PROTEIN  
 L51 3 S L49 NOT L50  
 L52 9 S L49 AND MUSCL?  
 L53 9 S L50,L51 AND L52  
 L54 5 S L49 NOT L53  
 L55 20 S L44,L53 AND L5-L12,L14,L15,L17-L20,L26-L54  
 L56 15 S L55 AND MUSCL?  
 L57 8 S L55 AND ?REGULAT?  
 L58 20 S L55-L57

FILE 'HCAPLUS' ENTERED AT 13:46:31 ON 02 FEB 2003

=> d all tot 158

L58 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2002:696465 HCAPLUS  
 DN 137:231356  
 TI Turkey **myostatin** for increasing **muscle** mass and testis  
 size as well as reducing body fat of livestock animals  
 IN El Halawani, Mohamed E.; You, Seungkwon  
 PA USA

SO U.S. Pat. Appl. Publ., 40 pp.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 IC ICM A61K039-00  
 NCL 424185100  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 2, 3, 5, 17

FAN.CNT 1

|    | PATENT NO.    | KIND | DATE     | APPLICATION NO.  | DATE         |  |
|----|---------------|------|----------|--|--------------|--|
| PI | US 2002127234 | A1   | 20020912 | US 2001-754826   | 20010104     |  |
|    | WO 2002094315 | A2   | 20021128 | WO 2002-US21862  | 20020104 <-- |  |
|    | W:            |      |          | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |              |  |
|    | RW:           |      |          | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |              |  |

PRAI US 2001-754826 A2 20010104 <--

AB A method to alter the phenotype of animals, e.g., avians, which employs passive and active **immunization** is provided. The method uses immunoconjugate of **myostatin** derived from an avian or vertebrate animal, esp. turkey, linked to a carrier such as keyhole limpet hemocyanin. The method may also use anti-**myostatin** antibodies for passive **immunization** of livestock animals, esp. turkey, chicken or pig.

ST turkey **myostatin** muscle mass testis size livestock animal

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(1; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(3; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(4; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(5; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

IT Bone morphogenetic proteins

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(7; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)

- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(CP-1; turkey **myostatin** for increasing **muscle** mass  
and testis size as well as reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-1 or growth/differentiation factor 1; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-10 or growth/differentiation factor 10; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-11 or growth/differentiation factor 11; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-2 or growth/differentiation factor 2; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-3 or growth/differentiation factor 3; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-4 or growth/differentiation factor 4; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-5 or growth/differentiation factor 5; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-6 or growth/differentiation factor 6; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-7 or growth/differentiation factor 7; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(GDF-9 or growth/differentiation factor 9; turkey **myostatin**

- for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Cytokines  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(MIC-1; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Growth factors, animal  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(MIS or Mullerian duct-inhibiting substance; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Proteins  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(Vgr-1 (Vgl-related); turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Antibodies  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(anti-idiotypic; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Drug delivery systems  
(carriers; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Human  
(consumption; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Immunoglobulins  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(fragments; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Aves  
(game bird; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Fissurella  
(hemocyanin; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Drug delivery systems  
(immunoconjugates; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Hemocyanins  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(keyhole limpet; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Cytokines  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(macrophage inhibition cytokine; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT **Muscle**  
(mass increase; turkey **myostatin** for increasing **muscle** mass and testis size as well as reducing body fat of livestock animals)
- IT Antibodies

RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (monoclonal; turkey **myostatin** for increasing **muscle**  
 mass and testis size as well as reducing body fat of livestock animals)

IT **Immunization**  
 (passive; turkey **myostatin** for increasing **muscle**  
 mass and testis size as well as reducing body fat of livestock animals)

IT Adipose tissue  
 (redn.; turkey **myostatin** for increasing **muscle** mass  
 and testis size as well as reducing body fat of livestock animals)

IT Testis  
 (size increase; turkey **myostatin** for increasing  
**muscle** mass and testis size as well as reducing body fat of  
 livestock animals)

IT Animal  
 Aquatic animal  
 Aves  
 Cattle  
 Chicken (Gallus domesticus)  
 Crustacea  
 DNA sequences  
 Feed  
 Fertilization  
 Fish  
 Goat  
 Horse (Equus caballus)  
**Immunization**  
 Livestock  
 Lobster  
 Mammalia  
 Molecular cloning  
 Phenotypes  
 Protein sequences  
 Sheep  
 Shrimp  
 Struthio camelus  
 Swine  
 Turkey  
**Vaccines**  
 Vertebrata  
 (turkey **myostatin** for increasing **muscle** mass and  
 testis size as well as reducing body fat of livestock animals)

IT Antibodies  
 Bone morphogenetic proteins  
 Fusion proteins (**chimeric** proteins)  
 RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (turkey **myostatin** for increasing **muscle** mass and  
 testis size as well as reducing body fat of livestock animals)

IT Aves  
 (waterfowl; turkey **myostatin** for increasing **muscle**  
 mass and testis size as well as reducing body fat of livestock animals)

IT Transforming growth factors  
 RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (.beta.-; turkey **myostatin** for increasing **muscle**  
 mass and testis size as well as reducing body fat of livestock animals)

IT Transforming growth factors  
 RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (.beta.1-; turkey **myostatin** for increasing **muscle**  
 mass and testis size as well as reducing body fat of livestock animals)

IT Transforming growth factors



RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(.beta.2-; turkey **myostatin** for increasing **muscle**  
mass and testis size as well as reducing body fat of livestock animals)

IT Transforming growth factors  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(.beta.3-; turkey **myostatin** for increasing **muscle**  
mass and testis size as well as reducing body fat of livestock animals)

IT **457995-62-9P, Growth/differentiation factor 8** (turkey)  
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); FFD (Food or  
feed use); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(amino acid sequence; turkey **myostatin** for increasing  
**muscle** mass and testis size as well as reducing body fat of  
livestock animals)

IT **457995-61-8P**  
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); FFD (Food or  
feed use); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(nucleotide sequence; turkey **myostatin** for increasing  
**muscle** mass and testis size as well as reducing body fat of  
livestock animals)

IT 114949-22-3D, Activin, analogs 117628-82-7, Follistatin  
**271597-12-7, Growth/differentiation factor 8**  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(turkey **myostatin** for increasing **muscle** mass and  
testis size as well as reducing body fat of livestock animals)

IT 458061-51-3  
RL: PRP (Properties)  
(unclaimed protein sequence; turkey **myostatin** for increasing  
**muscle** mass and testis size as well as reducing body fat of  
livestock animals)

IT 457878-13-6 457878-15-8 457878-17-0  
RL: PRP (Properties)  
(unclaimed sequence; turkey **myostatin** for increasing  
**muscle** mass and testis size as well as reducing body fat of  
livestock animals)

IT 57285-09-3D, Inhibin, analogs  
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use);  
BIOL (Biological study); USES (Uses)  
(.alpha., .beta.-.alpha., and .beta.-.beta.; turkey **myostatin**  
for increasing **muscle** mass and testis size as well as  
reducing body fat of livestock animals)

L58 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
AN 2002:676196 HCAPLUS  
DN 137:212638  
TI cDNA and protein sequence of inhibitors of **growth**  
**differentiation factor-8** (GDF-  
8) proteins of human and methods for their use  
IN Wolfman, Neil M.; Khor, Soo Peang  
PA Wyeth, John, and Brother Ltd., USA  
SO PCT Int. Appl., 109 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C12N015-12  
ICS C07K014-475; C07K014-51; C12N015-62; A61K038-18; A61P021-00;  
A61P003-00; A61P019-10

CC 6-3 (General Biochemistry)  
 Section cross-reference(s): 1, 3, 13, 14

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|----|--|------|----------|-----------------|--------------|
| PI | WO 2002068650  | A2   | 20020906 | WO 2002-US3467  | 20020208 <-- |
|    | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,<br>PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,<br>UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,<br>CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,<br>BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |      |          |                 |              |

PRAI US 2001-267509P P 20010208 <--

AB This invention relates to inhibitors of **Growth**

**Differentiation Factor-8 (GDF-**

**8)** proteins and methods for their use. The cDNA and protein sequence of **modified** and stabilized propeptides of human

**Growth Differentiation Factor** proteins, such

as **GDF-8** and Bone Morphogenetic Protein-11, are

disclosed. Also disclosed are methods for making and using the

**modified** propeptides to prevent or treat human or animal disorders

in which an increase in **muscle** tissue would be therapeutically

beneficial. Such disorders include **muscle** or neuromuscular

disorders (such as amyotrophic lateral sclerosis, muscular dystrophy,

**muscle** atrophy, congestive obstructive pulmonary disease,

**muscle** wasting syndrome, sarcopenia, or cachexia), metabolic

diseases or disorders (such as type 2 diabetes, noninsulin-dependent

diabetes mellitus, hyperglycemia, or obesity), adipose tissue disorders

(such as obesity) and bone degenerative diseases (such as osteoporosis).

ST human growth differentiation factor GDF8 cDNA sequence; bone morphogenic protein BMP11 cDNA sequence human; IgG Fc region sequence human disease drug

IT Fusion proteins (**chimeric** proteins)

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(BMP-11 fused to stabilizer portion; cDNA and protein sequence of

inhibitors of **growth differentiation factor**

**-8 (GDF-8)** proteins of human and methods

for their use)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(G, fusion products, **GDF-8** and BMP-11 propeptide

fused to Fc region of IgG via linker peptide; cDNA and protein sequence

of inhibitors of **growth differentiation**

**factor-8 (GDF-8)** proteins of

human and methods for their use)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(G1; cDNA and protein sequence of inhibitors of **growth**

**differentiation factor-8 (GDF-**

**8)** proteins of human and methods for their use)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(G4; cDNA and protein sequence of inhibitors of **growth**

**differentiation factor-8 (GDF-**

**8)** proteins of human and methods for their use)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(G; cDNA and protein sequence of inhibitors of **growth**



- differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**GDF-8 (growth differentiation factor)**); cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Immunoglobulin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (IgG, Fc region, stabilizer portion; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Bone morphogenetic proteins  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(MPP-11; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Nervous system  
(amyotrophic lateral sclerosis; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT **Muscle, disease**  
(atrophy; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Bone, disease  
(bone degenerative disease; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Cachexia  
Drug screening  
Human  
**Muscle, disease**  
Muscular dystrophy  
Neuromuscular diseases  
Obesity  
Osteoporosis  
Protein sequences  
Therapy  
cDNA sequences  
(cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Lung, disease  
(congestive obstructive; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Adipose tissue  
(disease; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Metabolism, animal  
(disorder; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Oligonucleotides  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(double stranded, encoding linker peptide; cDNA and protein sequence of

- inhibitors of **growth differentiation factor -8 (GDF-8)** proteins of human and methods for their use)
- IT Protein motifs  
(glycosylation site, alteration of, **GDF-8** and **BMP-11** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Mutation  
(in proteolytic cleavage site, of **modified GDF-8** and **BMP-11** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor -8 (GDF-8)** proteins of human and methods for their use)
- IT Protein motifs  
(inactivated proteolytic cleavage site, of **modified GDF-8** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor -8 (GDF-8)** proteins of human and methods for their use)
- IT Protein degradation  
(inhibition, of **modified GDF-8** and **BMP-11** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (linker, **GSGS** (glycine-serine-glycine-serine); cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Drugs  
(**modified GDF-8** and **BMP-11** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT cDNA  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**modified GDF-8** and **BMP-11** propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**modified, GDF-8** propeptide, half-life of; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Carbohydrates, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (moiety, **GDF-8** and **BMP-11** propeptide comprises; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Diabetes mellitus  
(non-insulin-dependent; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)
- IT Polymers, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (nonproteinaceous, stabilizer portion comprises of; cDNA and protein

sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Mutation**

(point, in modified **GDF-8** and BMP-11 propeptide; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Proteins**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(proproteins, **GDF-8** and BMP-11; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Proteins**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**recombinant, GDF-8** propeptide with Fc region of IgG; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Cell**

(**recombinant**; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Disease, animal**

(sarcopenia; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Albumins, biological studies**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (stabilizer portion of **modified GDF-8** propeptide, comprises of; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Purification**

(tag, **modified GDF-8** and BMP-11 propeptide comprises a; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT **Muscle, disease**

(wasting; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT 456540-96-8

RL: PRP (Properties)

(Unclaimed; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT 456538-28-6 456538-31-1

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT 456538-33-3, Immunoglobulin G (human Fc region) 456538-34-4

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8 (GDF-8)** proteins of human and methods for their use)

IT 456538-30-0 456538-32-2

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(nucleotide sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8** (GDF-8) proteins of human and methods for their use)

IT 456538-27-5 456538-29-7  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8** (GDF-8) proteins of human and methods for their use)

IT 456540-98-0, 3: PN: WO02068650 SEQID: 4 unclaimed DNA 456541-01-8  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8** (GDF-8) proteins of human and methods for their use)

IT 456540-97-9 456540-99-1 456541-00-7  
RL: PRP (Properties)  
(unclaimed protein sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8** (GDF-8) proteins of human and methods for their use)

IT 456527-91-6 456527-92-7  
RL: PRP (Properties)  
(unclaimed sequence; cDNA and protein sequence of inhibitors of **growth differentiation factor-8** (GDF-8) proteins of human and methods for their use)

L58 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
AN 2001:712046 HCAPLUS  
DN 136:19078  
TI Active vaccination against IL-5 bypasses immunological tolerance and ameliorates experimental asthma  
AU Hertz, Marc; Mahalingam, Surendran; Dalum, Iben; **Klysner, Steen**; Mattes, Joerg; Neisig, Anne; **Mouritsen, Soren**; Foster, Paul S.; Gautam, Anand  
CS Pharmexa A/S, Horsholm, DK-2970, Den.  
SO Journal of Immunology (2001), 167(7), 3792-3799  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
CC 15-9 (Immunochemistry)  
AB Current therapeutic approaches to asthma have had limited impact on the clin. management and resolu. of this disorder. By using a novel vaccine strategy targeting the inflammatory cytokine IL-5, the authors have ameliorated hallmark features of asthma in mouse models. Delivery of a DNA vaccine encoding murine IL-5 modified to contain a promiscuous foreign Th epitope bypasses B cell tolerance to IL-5 and induces neutralizing polyclonal anti-IL-5 Abs. Active vaccination against IL-5 reduces airways inflammation and prevents the development of eosinophilia, both hallmark features of asthma in animal models and humans. The reduced nos. of inflammatory T cells and eosinophils in the lung also result in a marked redn. of Th2 cytokine levels. Th-modified IL-5 DNA vaccination reduces the expression of IL-5 and IL-4 by .apprx.50% in the airways of allergen-challenged mice. Most importantly, Th-modified IL-5 DNA vaccination restores normal bronchial hyperresponsiveness to .beta.-methacholine. Active vaccination against IL-5 reduces key pathol. events assocd. with asthma, such as Th2 cytokine prodn., airways inflammation, and hyperresponsiveness, and thus represents a novel therapeutic approach for the treatment of asthma and other allergic conditions.

ST vaccine interleukin 5 asthma

- IT Gene therapy  
(DNA vaccine with IL-5 and tetanus toxoids help epitope bypasses immunol. tolerance and ameliorates exptl. asthma)
- IT Vaccines  
(DNA; active vaccination against IL-5 bypasses immunol. tolerance and ameliorates exptl. asthma)
- IT B cell (lymphocyte)  
(active vaccination against IL-5 bypasses B cell tolerance and ameliorates exptl. asthma)
- IT Asthma  
Immune tolerance  
(active vaccination against IL-5 bypasses immunol. tolerance and ameliorates exptl. asthma)
- IT Eosinophilia  
(active vaccination against IL-5 reduces airways inflammation and prevents the development of eosinophilia)
- IT T cell (lymphocyte)  
(active vaccination against IL-5 reduces inflammatory T cells)
- IT Interleukin 10  
Interleukin 4  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(active vaccination against IL-5 reduces inflammatory T cells and Th2 cytokine levels)
- IT Interleukin 5  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fusion product with tetanus toxoid help epitope; active vaccination against IL-5 bypasses immunol. tolerance and ameliorates exptl. asthma)
- IT T cell (lymphocyte)  
(helper cell/inducer, TH2; active vaccination against IL-5 reduces inflammatory T cells and Th2 cytokine levels)
- IT Bronchi  
(hyperresponsiveness; Th-modified IL-5 DNA vaccination restores normal bronchial hyperresponsiveness)
- IT Lung, disease  
(inflammation; active vaccination against IL-5 reduces airways inflammation and prevents the development of eosinophilia)
- IT Toxoids  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tetanus, helper epitope; fusion product with interleukin-5; DNA vaccine with IL-5 and tetanus toxoids bypasses immunol. tolerance and ameliorates exptl. asthma)
- IT **126779-14-4**  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fusion product with interleukin-5; DNA vaccine with IL-5 and tetanus toxoids help epitope bypasses immunol. tolerance and ameliorates exptl. asthma)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Akutsu, I; Immunol Lett 1995, V45, P109 HCAPLUS
- (2) Azzawi, M; Am Rev Respir Dis 1990, V142, P1407 MEDLINE
- (3) Beasley, R; Am Rev Respir Dis 1989, V139, P806 MEDLINE
- (4) Bousquet, J; N Engl J Med 1990, V323, P1033 MEDLINE
- (5) Broide, D; J Allergy Clin Immunol 1991, V88, P637 MEDLINE
- (6) Broide, D; J Immunol 1998, V161, P7054 HCAPLUS
- (7) Buhl, A; Immunol Rev 2000, V176, P141 HCAPLUS
- (8) Corry, D; J Exp Med 1996, V183, P109 HCAPLUS
- (9) Dalum, I; J Immunol 1996, V157, P4796 HCAPLUS
- (10) Dalum, I; Mol Immunol 1997, V34, P1113 HCAPLUS
- (11) Dalum, I; Nat Biotechnol 1999, V17, P666 HCAPLUS
- (12) De Monchy, J; Am Rev Respir Dis 1985, V131, P373 MEDLINE

- (13) Drazen, J; J Exp Med 1996, V183, P1 HCAPLUS
- (14) Egan, R; Int Arch Allergy Immunol 1995, V107, P321 MEDLINE
- (15) Foster, P; J Exp Med 1996, V183, P195 HCAPLUS
- (16) Goodnow, C; Proc Natl Acad Sci 1996, V93, P2264 HCAPLUS
- (17) Gulbenkian, A; Am Rev Respir Dis 1992, V146, P263 HCAPLUS
- (18) Hakonarson, H; J Clin Invest 1999, V103, P1077 HCAPLUS
- (19) Hakonarson, H; J Clin Invest 1999, V104, P657 HCAPLUS
- (20) Hamelmann, E; Am J Respir Crit Care Med 1997, V156, P766 MEDLINE
- (21) Hertz, M; Curr Opin Immunol 1998, V10, P208 HCAPLUS
- (22) Hogan, S; Am J Respir Crit Care Med 1998, V157, P210 MEDLINE
- (23) Hogan, S; J Immunol 1998, V161, P1501 HCAPLUS
- (24) Kline, J; J Immunol 1998, V160, P2555 HCAPLUS
- (25) Kozak, M; Nucleic Acids Res 1987, V15, P8125 HCAPLUS
- (26) Kung, T; Am J Respir Cell Mol Biol 1995, V13, P360 HCAPLUS
- (27) Leckie, M; Lancet 2000, V356, P2144 HCAPLUS
- (28) Mauser, P; Am J Respir Crit Care Med 1995, V152, P467 MEDLINE
- (29) Mauser, P; Am Rev Respir Dis 1993, V148, P1623 MEDLINE
- (30) Nagai, H; Life Sci 1993, V53, PL243
- (31) Nakajima, H; Am Rev Respir Dis 1992, V146, P374 HCAPLUS
- (32) Ohashi, Y; Am Rev Respir Dis 1992, V145, P1469 MEDLINE
- (33) Ohnishi, T; Am Rev Respir Dis 1993, V147, P901 HCAPLUS
- (34) Panina-Bordignon, P; Eur J Immunol 1989, V19, P2237 HCAPLUS
- (35) Robinson, D; J Allergy Clin Immunol 1993, V92, P313 MEDLINE
- (36) Robinson, D; J Allergy Clin Immunol 1993, V92, P397 MEDLINE
- (37) Robinson, D; N Engl J Med 1992, V326, P298 MEDLINE
- (38) Shardonofsky, F; J Allergy Clin Immunol 1999, V104, P215 HCAPLUS
- (39) Stamm, L; J Immunol 1998, V161, P6180 HCAPLUS
- (40) Sur, S; Allergy 1995, V50, P891 MEDLINE
- (41) Tournoy, K; J Immunol 2001, V166, P6982 HCAPLUS
- (42) Van Oosterhout, A; Am Rev Respir Dis 1993, V147, P548 HCAPLUS
- (43) Walker, C; Am Rev Respir Dis 1992, V146, P109 MEDLINE
- (44) Walker, C; J Allergy Clin Immunol 1991, V88, P935 MEDLINE
- (45) Wardlaw, A; Am Rev Respir Dis 1988, V137, P62 MEDLINE
- (46) Webb, D; J Immunol 2000, V165, P108 HCAPLUS
- (47) Wynn, T; J Immunol 1993, V151, P1430 HCAPLUS

L58 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:265459 HCAPLUS

DN 134:290751

TI **Recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders

IN **Halkier, Torben**; Schambye, Hans Thalsgard; Okkels, Jens Sigurd; Andersen, Kim Vilbour; Nissen, Torben Lauesgaard; Soni, Bobby; Jeppesen, Claus Bekker; Van Den Hazel, Bart

PA Maxygen Aps, Den.

SO PCT Int. Appl., 123 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-525

ICS A61K038-22; A61P029-00; C07K019-00; C07K001-107; C12N015-62; C07K014-52

CC 2-10 (Mammalian Hormones)

Section cross-reference(s): 1, 3

FAN.CNT 1

|    | PATENT NO.    | KIND  | DATE     | APPLICATION NO. | DATE         |
|----|---------------|---|----------|-----------------|--------------|
| PI | WO 2001025277 | A1  | 20010412 | WO 2000-DK563   | 20001006 <-- |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, |          |                 |              |



ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1226173 A1 20020731 EP 2000-965860 20001006 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL  
 PRAI DK 1999-1438 A 19991007 <--  
 DK 1999-1855 A 19991223 <--  
 DK 2000-1119 A 20000720 <--  
 WO 2000-DK563 W 20001006 <--  
 AB The invention relates to a single-chain oligomeric protein antagonist  
 which binds to an extracellular ligand-binding domain of a cellular  
 receptor of a type requiring binding of an oligomeric ligand to two or  
 more receptor subunits to be activated, the protein comprising at least  
 two, typically structurally homologous, receptor-binding sites of which at  
 least one is capable of binding to a ligand-binding domain of the cellular  
 receptor and at least one is incapable of effectively binding to a  
 ligand-binding domain of the cellular receptor, whereby the single-chain  
 oligomeric protein is capable of binding to the receptor, but incapable of  
 activating the receptor; as well as to nucleotide sequences encoding such  
 single-chain oligomeric proteins, expression vectors comprising such a  
 nucleotide sequence, **recombinant** host cells comprising such a  
 nucleotide sequence or expression vector, methods for producing the  
 nucleotide sequences and proteins, pharmaceutical compns. comprising the  
 single-chain oligomeric protein, and use of the single-chain oligomeric  
 protein for the prodn. of medicaments and in therapy. A preferred  
 single-chain antagonist according to the invention is a TNF-.alpha.  
 antagonist. Thus, a single-chain TNF-.alpha. protein comprising of 3  
 human TNF-.alpha. chains connected by linker peptides was produced with  
 Saccharomyces cerevisiae and shown to be an agonist of the TNF-.alpha.  
 receptor. The same TNF-.alpha. trimer contg. Y87R **mutations** in  
 the first and third copies of TNF-.alpha. was also prepd. This was shown  
 to be a partial TNF-.alpha. agonist and a competitive antagonist of the  
 TNF-.alpha. receptor.  
 ST single chain tumor necrosis factor alpha trimer **recombinant**; TNF  
 alpha receptor antagonist single chain trimer ligand  
 IT Bone morphogenetic proteins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (2, single-chain multimers; **recombinant** single-chain receptor  
 antagonist proteins and their use in treatment of inflammatory  
 disorders)  
 IT Bone morphogenetic proteins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (3, single-chain multimers; **recombinant** single-chain receptor  
 antagonist proteins and their use in treatment of inflammatory  
 disorders)  
 IT Bone morphogenetic proteins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (4, single-chain multimers; **recombinant** single-chain receptor  
 antagonist proteins and their use in treatment of inflammatory  
 disorders)  
 IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (4-1BB ligand, single-chain multimers; **recombinant**

- single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Bone morphogenetic proteins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(5, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Bone morphogenetic proteins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(6, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Bone morphogenetic proteins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(7, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Bone morphogenetic proteins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(8, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Cytokines  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(APRIL, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT CD antigens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CD27, ligand, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Glycoproteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CD40-L (antigen CD40 ligand), single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Intestine, disease  
(Crohn's; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Antigens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(OX-40, ligand, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

- study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (PIGF, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (TRAIL (tumor necrosis factor-related apoptosis-inducing ligand), single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Granulomatous disease  
 (Wegener's granulomatosis; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Spinal column  
 (ankylosing spondylitis; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Antiarteriosclerotics  
 (antiatherosclerotics; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (death domain; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Heart, disease  
 (infarction; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Brain, disease  
 (injury; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT CD30 (antigen)  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ligand, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Molecular cloning  
 (of single-chain antagonist protein DNA; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Tumor necrosis factor receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (p55; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Tumor necrosis factor receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (p75; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Arthritis  
 (psoriatic arthritis; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Anti-inflammatory agents  
 Antirheumatic agents

Cachexia  
Diabetes mellitus  
Myasthenia gravis  
Psoriasis  
Sjogren's syndrome

(**recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Cytokine receptors

Growth factor receptors

Tumor necrosis factor receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Shock (circulatory collapse)

(septic; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Lymphotoxin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(single-chain multimers contg. .alpha. and .beta. chains of; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Fas ligand

Interleukin 10

Interleukin 16

Platelet-derived growth factors

Tumor necrosis factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Surgery

(stress from; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Lupus erythematosus

(systemic; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Eye, disease

(uveitis; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(with Tyr or Ser/Thr protein kinase activity; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Transforming growth factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.1-, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

IT Transforming growth factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.2-, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)

- disorders)
- IT Transforming growth factors  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.3-, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Transforming growth factors  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.4-, single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT Interferons  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.gamma., single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 334838-89-0P  
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)  
(amino acid sequence; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 334838-90-3P  
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 334838-88-9  
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 9026-43-1, Serine-threonine kinase 80449-02-1, Protein tyrosine kinase  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(receptors; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 80497-65-0, Muellierian inhibiting factor 102510-92-9, Inhibin A 104625-48-1, Activin A 114949-23-4, Activin AB 115088-91-0, Inhibin B 127464-60-2, Vascular endothelial growth factor 188417-84-7, VEGF C 192662-83-2, Vascular endothelial growth factor B 193363-12-1, VEGF-D 193830-08-9, Growth/differentiation factor 5 207621-35-0, TRANCE 271597-10-5, Growth/differentiation factor 1 **271597-12-7, Growth/differentiation factor 8** 271597-13-8, Growth/differentiation factor 10  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(single-chain multimers; **recombinant** single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders)
- IT 334845-12-4, 6: PN: WO0125434 FIGURE: 4 unclaimed DNA



RL: PRP (Properties)  
 (unclaimed nucleotide sequence; **recombinant** single-chain  
 receptor antagonist proteins and their use in treatment of inflammatory  
 disorders)

IT 115089-05-9, 28-171-Lymphotoxin (human protein moiety) 147681-94-5,  
 Lymphotoxin .beta. (human II-23.D7 cell) 334845-09-9 334845-10-2  
 334845-11-3

RL: PRP (Properties)  
 (unclaimed protein sequence; **recombinant** single-chain  
 receptor antagonist proteins and their use in treatment of inflammatory  
 disorders)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE

- (1) Angeletti P Ist Recherche Bio; WO 9709064 A 1997 HCAPLUS
- (2) Biogen Inc; WO 9640774 A 1996 HCAPLUS
- (3) Economides, A; US 5844099 A 1998 HCAPLUS
- (4) Howl, J; FASEB JOURNAL 1997, V11(7), P582 MEDLINE
- (5) Johnson & Johnson; WO 9640772 A 1996 HCAPLUS
- (6) Kyowa Hakko Kogyo Kk; EP 0370205 A 1990 HCAPLUS
- (7) McKinnon, M; DRUG NEWS AND PERSPECTIVES, XX, XX 1996, V9, P389 HCAPLUS
- (8) Smithkline Beecham Corp; WO 9952877 A 1999 HCAPLUS
- (9) Strominger, J; WO 9805684 A 1998 HCAPLUS
- (10) Univ Helsinki Licensing; WO 9833917 A 1998 HCAPLUS
- (11) Yeda Res & Dev; EP 0526905 A 1993 HCAPLUS

L58 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:64021 HCAPLUS

DN 134:130255

TI Method for **down-regulating GDF-8**  
 activity

IN **Halkier, Torben; Mouritsen, Soren; Klysner, Steen**

PA M and E Biotech A/S, Den.

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-00

CC 15-2 (Immunochemistry)

Section cross-reference(s): 2, 3, 5, 63

FAN.CNT 1

|      | PATENT NO.   | KIND   | DATE     | APPLICATION NO. | DATE         |
|------|--|--|----------|-----------------|--------------|
| PI   | WO 2001005820  | A2   | 20010125 | WO 2000-DK413   | 20000720 <-- |
|      | WO 2001005820  | A3   | 20010719 |                 |              |
|      | W:   | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |              |
|      | RW:  | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |              |
|      | EP 1200119   | A2   | 20020502 | EP 2000-945671  | 20000720 <-- |
|      | R:   | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL   |          |                 |              |
|      | NO 2001006252  | A  | 20020315 | NO 2001-6252    | 20011219 <-- |
| PRAI | DK 1999-1014   | A  | 19990720 | <--             |              |
|      | US 1999-145275P  | P  | 19990726 | <--             |              |
|      | WO 2000-DK413  | W  | 20000720 | <--             |              |
| AB   | Disclosed are novel methods for increasing <b>muscle</b> mass by means |  |          |                 |              |



of immunization against **growth differentiation factor 8 (GDF-8, myostatin)**. Immunization is preferably effected by administration of analogs of **GDF-8** which are capable of inducing antibody prodn. against homologous **GDF-8**. Esp. preferred as an immunogen is homologous **GDF-8** which has been **modified** by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes while substantially preserving the tertiary structure of the homologous **GDF-8**. Also disclosed are nucleic acid **vaccination** against **GDF-8** and **vaccination** using live **vaccines** as well as methods and means useful for the **vaccination**. Such methods and means include methods for identification of useful immunogenic **GDF-8** analogs, methods for the prepn. of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

ST **growth differentiation factor 8**

**muscle** mass; **vaccine** GDF8 farm animal **muscle** mass

IT Antigen

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CS (circumsporozoite); **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Hematopoietin receptors

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(FLT3 receptors; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Heat-shock proteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HSP 70; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Heat-shock proteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HSP 90; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Histocompatibility antigens

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MHC (major histocompatibility complex), class II; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Diglycerides

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(N-acyl; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Proteins, specific or class

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(P2; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

- IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(P30; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Animal cell line  
(S2; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Animal cell line  
(SF; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Encapsulants  
(adjuvant; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT DNA  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(adjuvant; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Immunostimulants  
(adjuvants, ISCOMs; **chimeric vaccines** for  
**down-regulation** of GDF-8 activity  
and for increase of **muscle** mass in farm animals)
- IT Immunostimulants  
(adjuvants; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(anal; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Immune tolerance  
(auto-; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(autoantigens; **chimeric vaccines** for down  
**-regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(buccal; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Reagents  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(calcium-pptg.; **chimeric vaccines** for down  
**-regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(carriers; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Animal  
Animal cell line  
Antigen-presenting cell

B cell (lymphocyte)  
 Bacillus (bacterium genus)  
 Bacteriophage  
 Bacterium (genus)  
 Cattle  
 Chicken (Gallus domesticus)  
 Cosmids  
 Epitopes  
 Escherichia  
 Escherichia coli  
 Eukaryote (Eukaryotae)  
 Fungi  
 Genetic vectors  
 Genome  
 Immunostimulants  
 Influenza virus  
 Insect (Insecta)  
 Livestock  
 Micelles  
 Microorganism  
 Mycobacterium  
 Mycobacterium bovis  
 Particles  
 Plant cell  
 Plasmids  
 Plasmodium falciparum  
 Poultry  
 Poxviridae  
 Prokaryote  
 Protein sequences  
 Protozoa  
 Salmonella  
 Sheep  
 Swine  
 Turkey

#### **Vaccines**

**Vaccinia** virus

Virus vectors

Yeast

(chimeric vaccines for down-  
 regulation of GDF-8 activity and for  
 increase of muscle mass in farm animals)

IT Antibodies

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)

(chimeric vaccines for down-  
 regulation of GDF-8 activity and for  
 increase of muscle mass in farm animals)

IT Fusion proteins (chimeric proteins)

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);  
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

(chimeric vaccines for down-  
 regulation of GDF-8 activity and for  
 increase of muscle mass in farm animals)

IT Calreticulin

Carbohydrates, biological studies

Cytokines

Haptens

Heat-shock proteins

Hemagglutinins

Hormones, animal, biological studies

Interleukin 1

Interleukin 12

Interleukin 13

Interleukin 15

Interleukin 2

Interleukin 4

Interleukin 6

Leader peptides

Lipids, biological studies

Nucleic acids

Polymers, biological studies

Promoter (genetic element)

Receptors

Saponins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(**chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT **Mutation**

(**deletion**; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Toxoids

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(diphtheria; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Glycophosphoproteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(endoplasmins; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems

(epidural; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT T cell (lymphocyte)

(epitope; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT T cell (lymphocyte)

(helper cell, epitope; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Phosphoproteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(hsc 70 (heat-shock cognate, 70,000-mol.-wt.); **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Carriers

Molecules

(inert; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems

(injections, i.m.; **chimeric vaccines** for **down-regulation** of **GDF-8** activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems

(injections, i.v.; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(injections, s.c.; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT **Mutation**  
(insertion; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(intraarterial; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(intracranial; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(intracutaneous; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(intradermal; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(liposomes; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Animal cell  
(mammalian; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT **Muscle**  
(mass; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Chromosome  
(minichromosomes; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(oil formulation; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(oral; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(parenterals; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Drug delivery systems  
(peritoneal; **chimeric vaccines** for down-regulation of GDF-8 activity and for increase of **muscle** mass in farm animals)

IT Glycolipoproteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(phosphatidylinositol-contg.; **chimeric vaccines** for

- down-regulation of GDF-8 activity  
and for increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(spinal; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(subdermal; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Drug delivery systems  
(sublingual; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT **Mutation**  
(substitution; **chimeric vaccines** for  
**down-regulation** of GDF-8 activity  
and for increase of **muscle** mass in farm animals)
- IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(surface; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Genetic element  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(terminator; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Toxoids  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(tetanus; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(transfection-facilitating; **chimeric vaccines** for  
**down-regulation** of GDF-8 activity  
and for increase of **muscle** mass in farm animals)
- IT Lymph node  
(virtual lymph node device; **chimeric vaccines** for  
**down-regulation** of GDF-8 activity  
and for increase of **muscle** mass in farm animals)
- IT Interferons  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(.gamma.; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT 7429-90-5D, Aluminum, derivs., biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(adjuvant; **chimeric vaccines** for down-  
**regulation** of GDF-8 activity and for  
increase of **muscle** mass in farm animals)
- IT 161135-86-0, Growth/differentiation  
factor 8 (human) 211433-36-2, Growth  
/differentiation factor 8 (cattle)  
321893-41-8 321893-42-9 321893-43-0  
321893-44-1 321893-45-2 321893-46-3



- 321893-47-4 321893-48-5 321893-49-6  
 321893-50-9 321893-51-0  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (amino acid sequence; **chimeric vaccines** for  
**down-regulation** of GDF-8 activity  
 and for increase of **muscle** mass in farm animals)
- IT 271597-12-7, **Growth differentiation factor 8** 321856-81-9 321856-82-0  
 321856-83-1 321856-84-2 321856-85-3  
 321856-86-4 321856-87-5 321856-88-6  
 321856-89-7 321856-90-0 321856-91-1  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**chimeric vaccines** for **down-regulation** of GDF-8 activity and for  
 increase of **muscle** mass in farm animals)
- IT 112-18-5, DDA 1398-61-4, Chitin 3458-28-4, Mannose 9012-76-4,  
 Chitosan 9036-88-8, Mannan 83869-56-1, GM-CSF  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**chimeric vaccines** for **down-regulation** of GDF-8 activity and for  
 increase of **muscle** mass in farm animals)
- IT 7440-70-2, Calcium, biological studies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pptg. agent; **chimeric vaccines** for **down-regulation** of GDF-8 activity and for  
 increase of **muscle** mass in farm animals)
- IT 161135-84-8 199810-42-9, **Myostatin** (cattle **muscle** gene MSTN) 199810-43-0, **Myostatin**  
 (chicken **muscle** gene MSTN) 199810-44-1, **Myostatin** (sheep **muscle** gene MSTN) 199810-45-2  
 , **Myostatin** (swine **muscle** gene MSTN)  
 199810-46-3 199810-47-4, **Myostatin** (turkey **muscle** gene MSTN) 199810-48-5, **Myostatin**  
 (Danio rerio **muscle** gene MSTN)  
 RL: PRP (Properties)  
 (unclaimed protein sequence; method for **down-regulating** GDF-8 activity)
- IT 126779-13-3 126779-14-4  
 RL: PRP (Properties)  
 (unclaimed sequence; method for **down-regulating** GDF-8 activity)
- IT 9005-80-5, Inulin  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.gamma.-; **chimeric vaccines** for **down-regulation** of GDF-8 activity and for  
 increase of **muscle** mass in farm animals)
- L58 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2000:772763 HCAPLUS  
 DN 133:334046  
 TI Autovaccines for **down-regulating** interleukin 5 activity and  
 treatment of asthma and allergy  
 IN **Klysner, Steen**  
 PA M & E Biotech A/S, Den.  
 SO PCT Int. Appl., 172 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English

IC ICM C12N015-24  
 ICS A61K039-00; A61K039-385; A61K039-39; A61K031-70; A61K048-00;  
 C07K014-54; C12N001-21; C12N001-19; C12N005-10; C12N015-70;  
 C12N015-86; G01N033-68; A61P037-00; A61K039-08

CC 15-2 (Immunochemistry)

FAN.CNT 1

|      | PATENT NO.      | KIND | DATE     | APPLICATION NO.  | DATE         |  |
|------|-----------------|------|----------|--|--------------|--|
| PI   | WO 2000065058   | A1   | 20001102 | WO 2000-DK205  | 20000419 <-- |  |
|      | W:              |      |          | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |              |  |
|      | RW:             |      |          | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |              |  |
|      | EP 1173573      | A1   | 20020123 | EP 2000-920423   | 20000419 <-- |  |
|      | R:              |      |          | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |              |  |
|      | NO 2001005021   | A    | 20011221 | NO 2001-5021   | 20011015 <-- |  |
| PRAI | DK 1999-552     | A    | 19990423 |  | <--          |  |
|      | US 1999-132811P | P    | 19990506 |  | <--          |  |
|      | WO 2000-DK205   | W    | 20000419 |  | <--          |  |

AB The present invention relates to improvements in therapy and prevention of conditions characterized by an elevated level of eosinophil leukocytes, i.e., conditions such as asthma and other chronic allergic diseases. A method is provided for down-regulating interleukin 5 (IL5) by enabling the prodn. of antibodies against IL5 thereby reducing the level of activity of eosinophils. The invention also provides for methods of producing modified IL5 useful in this method as well as for the modified IL5 as such. Also encompassed by the present invention are nucleic acid fragments encoding modified IL5 as well as vectors incorporating these nucleic acid fragments and host cells and cell lines transformed therewith. The invention also provides for a method for the identification of IL5 analogs which are useful in the method of the invention as well as for compns. comprising modified IL5 or comprising nucleic acids encoding the IL5 analogs. The preferred embodiment of the present invention entails the use of variants of IL5, where foreign T helper epitopes are introduced so as to induce prodn. of cross-reactive antibodies capable of binding to autologous IL5. Thus, genes encoding human and mouse IL5 with tetanus toxoid P2 or P30 epitope replacing loops 1, 2 or 3 were prepd. These genes were expressed in Drosophila S2 cells. Both protein and DNA were used to vaccinate mice. Anti-IL5 antibodies were produced.

ST autovaccine interleukin 5 tetanus toxoid chimera asthma allergy treatment  
 IT Antigens

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (CS (circumsporozoite), interleukin 5 analog contg. epitope of P. falciparum; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

IT Hematopoietin receptors  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (FLT3 receptors, interleukin 5 analog contg. ligand for; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

IT Heat-shock proteins  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (HSP 70, interleukin 5 analog contg.; autovaccines for down-

- regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Heat-shock proteins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(HSP 90, interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Interleukin 5  
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(analogs; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Allergy inhibitors  
Antiasthmatics  
Vaccines  
(autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Interleukin 5  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Toxoids  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(diphtheria, interleukin 5 analog contg. epitope of; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Glycophosphoproteins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(endoplasmins, interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Gene  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(for interleukin 5 analog; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT T cell (lymphocyte)  
(helper cell, interleukin 5 analog contg. target for; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Phosphoproteins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(hsc 70 (heat-shock cognate, 70,000-mol.-wt.), interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Hemagglutinins  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(interleukin 5 analog contg. epitope of flu virus; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)
- IT Antigen-presenting cell  
B cell (lymphocyte)  
(interleukin 5 analog contg. target for; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and

allergy)

IT Immunostimulants  
(interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Calreticulin  
Cytokines  
Heat-shock proteins  
Hormones, animal, biological studies  
Interleukin 1  
Interleukin 12  
Interleukin 13  
Interleukin 15  
Interleukin 2  
Interleukin 4  
Interleukin 6  
Lipids, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Genetic vectors  
(interleukin 5 analog-encoding; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Animal cell line  
Bacillus (bacterium genus)  
Cell  
Escherichia  
Escherichia coli  
Mycobacterium  
Mycobacterium BCG  
Salmonella  
(interleukin 5 analog-producing; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT DNA sequences  
(of genes for human and mouse interleukin 5-tetanus toxoid fusion proteins)

IT Protein sequences  
(of human and mouse interleukin 5-tetanus toxoid fusion proteins)

IT Antigens  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(surface, interleukin 5 analog contg. binding partner for B cell or APC; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Toxoids  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(tetanus, interleukin 5 analog contg. epitope of; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Vaccinia virus  
(vector, interleukin 5 analog-encoding; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT Interferons  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(.gamma., interleukin 5 analog contg.; autovaccines for down-**regulating** interleukin 5 activity and treatment of asthma and allergy)

IT 126779-13-3 126779-14-4 303779-77-3

RL: PRP (Properties)  
(Unclaimed; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

IT 303810-21-1P 303810-22-2P 303810-23-3P 303810-24-4P 303810-25-5P  
303810-26-6P 303810-27-7P 303810-28-8P 303810-29-9P 303810-30-2P  
303810-32-4P 303810-33-5P 303810-34-6P 303810-35-7P 303810-36-8P  
303810-37-9P 303810-38-0P 303810-39-1P 303810-40-4P 303810-41-5P  
303810-60-8P 303810-67-5P 303810-69-7P 303810-71-1P 303810-73-3P  
303810-79-9P 303810-81-3P 303810-83-5P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; of genes for human and mouse interleukin 5-tetanus toxoid fusion proteins)

IT 112759-45-2DP, Interleukin 5 (human clone pEDFH-1 protein moiety reduced), analogs 303810-31-3DP, Interleukin 5 (Mus musculus), analogs  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; of genes for human and mouse interleukin 5-tetanus toxoid fusion proteins)

IT 57-10-3, Palmitic acid, biological studies 544-63-8, Myristic acid, biological studies 83869-56-1, GM-CSF  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(interleukin 5 analog contg.; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

IT 303810-59-5 303810-61-9 303810-62-0 303810-63-1 303810-64-2  
303810-65-3 303810-66-4 303810-68-6 303810-70-0 303810-72-2  
303810-74-4 303810-75-5 303810-76-6 303810-77-7 303810-78-8  
303810-80-2 303810-82-4  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; of genes for human and mouse interleukin 5-tetanus toxoid fusion proteins)

IT 264134-77-2 303815-99-8  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

IT 161147-59-7 303779-78-4  
RL: PRP (Properties)  
(unclaimed sequence; autovaccines for down-regulating interleukin 5 activity and treatment of asthma and allergy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Bresagen Ltd; WO 9745448 A 1997 HCAPLUS
- (2) Broide, D; JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, part 2 1997, V99(1), PS129
- (3) Commonwealth Scientific And Industrial Research Organisation; WO 9700321 A 1997 HCAPLUS
- (4) Mouritsen & Elsner AS; WO 9505849 A 1995 HCAPLUS
- (5) S P I Synthetic Peptides Inc; WO 9531480 A 1995 HCAPLUS
- (6) Takatsu, K; CYTOKINE AND GROWTH FACTOR REVIEWS 1998, V9(1), P25 HCAPLUS
- (7) Tanox Biosystems Inc; WO 9847923 A 1998 HCAPLUS
- (8) The Trustees Of The University Of Pennsylvania; WO 9817799 A 1998 HCAPLUS
- (9) United Biomedical Inc; WO 9526365 A 1995 HCAPLUS
- (10) Weltman, J; ALLERGY AND ASTHMA PROCEEDINGS 1998, V19(5), P257 HCAPLUS

L58 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
AN 2000:240985 HCAPLUS  
DN 132:292701  
TI Novel methods for therapeutic vaccination



IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious;  
 Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter;  
 Karlsson, Gunilla  
 PA M Amp E Biotech A/s, Den.  
 SO PCT Int. Appl., 220 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC A61K039-00  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 3, 63

FAN.CNT 1

|      | PATENT NO.      | KIND   | DATE     | APPLICATION NO. | DATE         |
|------|-----------------|--|----------|-----------------|--------------|
| PI   | WO 2000020027   | A2   | 20000413 | WO 1999-DK525   | 19991005 <-- |
|      | WO 2000020027   | A3   | 20001012 |                 |              |
|      | W:              | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |              |
|      | RW:             | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |              |
|      | CA 2345817      | AA   | 20000413 | CA 1999-2345817 | 19991005 <-- |
|      | AU 9958510      | A1   | 20000426 | AU 1999-58510   | 19991005 <-- |
|      | AU 751709       | B2   | 20020822 |                 |              |
|      | EP 1117421      | A2   | 20010725 | EP 1999-945967  | 19991005 <-- |
|      | R:              | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO   |          |                 |              |
|      | JP 2002526419   | T2   | 20020820 | JP 2000-573386  | 19991005 <-- |
|      | NO 2001001586   | A  | 20010531 | NO 2001-1586    | 20010328 <-- |
| PRAI | DK 1998-1261    | A  | 19981005 | <--             |              |
|      | US 1998-105011P | P  | 19981020 | <--             |              |
|      | WO 1999-DK525   | W  | 19991005 | <--             |              |

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

ST weak antigen vaccine cytotoxic T lymphocyte; tumor antigen T cell epitope vaccine

IT Antigens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (17-1A; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (AM-1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



(APC; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(APRIL; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BAGE; weak antigens inserted with foreign T cell epitope as vaccines)

IT Chemokines  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(C-X-C, Ena78; weak antigens inserted with foreign T cell epitope as vaccines)

IT CD antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CD33; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CD40-L (antigen CD40 ligand); weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CD52; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CDC27; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CO17-1A; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CS (circumsporozoite), epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DCC (deleted in colorectal cancer); weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DcR3; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(E6; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transcription factors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(E7; weak antigens inserted with foreign T cell epitope as vaccines)

IT Hematopoietin receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(FLT3 receptors; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(GP1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
(H-CAM (homing cell adhesion mol.); weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(H-ras; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HMTV; weak antigens inserted with foreign T cell epitope as vaccines)

IT Heat-shock proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HSP 70; weak antigens inserted with foreign T cell epitope as vaccines)

IT Heat-shock proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HSP 90; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunoglobulin receptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(IgE type II; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(K-ras; weak antigens inserted with foreign T cell epitope as vaccines)

IT Lipoprotein receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(LDL, fusion with FUT or fucosyltransferase; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(MCP (membrane cofactor protein); weak antigens inserted with foreign T cell epitope as vaccines)

IT Multidrug resistance proteins  
Multidrug resistance proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(MDR1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(MHC (major histocompatibility complex), class I; weak antigens inserted with foreign T cell epitope as vaccines)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(MHC (major histocompatibility complex), class II; weak antigens inserted with foreign T cell epitope as vaccines)

IT Diglycerides  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-acyl; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-ras; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
Glycoproteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(P170; weak antigens inserted with foreign T cell epitope as vaccines)

IT Phosphoproteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(P210bcr-c-abl; weak antigens inserted with foreign T cell epitope as vaccines)

IT Prostate-specific antigen  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(PSA and PSM; weak antigens inserted with foreign T cell epitope as vaccines)

IT Hemopoietins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Progenipoietin; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transcription factors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Rb; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(SART-1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Gene, animal  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(SSX; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transcription factors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(STAT3; weak antigens inserted with foreign T cell epitope as vaccines)

IT Mucins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(STn antigen; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(TAG-72 (tumor-assocd. glycoprotein 72); weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(TPA (tissue protein antigen); weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(TRP-1 (tyrosinase-related protein 1); weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(TRP-2 (tyrosinase-related protein 2); weak antigens inserted with foreign T cell epitope as vaccines)

IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adjuvant; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunostimulants  
(adjuvants, Freund's incomplete; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunostimulants  
(adjuvants, Freund's; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunostimulants  
(adjuvants, ISCOMs; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunostimulants  
(adjuvants, Ribi; weak antigens inserted with foreign T cell epitope as vaccines)

IT Immunostimulants  
(adjuvants; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems

(anal; weak antigens inserted with foreign T cell epitope as vaccines)

IT Animal virus  
Bacteria (Eubacteria)  
Parasite  
(antigen; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bcl-2; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems  
(buccal; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transcription factors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(c-myc; weak antigens inserted with foreign T cell epitope as vaccines)

IT Diagnosis  
(cancer; weak antigens inserted with foreign T cell epitope as vaccines)

IT T cell (lymphocyte)  
(cytotoxic, epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Mutation  
(deletion; weak antigens inserted with foreign T cell epitope as vaccines)

IT Neoplasm  
(diagnosis; weak antigens inserted with foreign T cell epitope as vaccines)

IT Toxoids  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(diphtheria, epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycophosphoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(endoplasmins; weak antigens inserted with foreign T cell epitope as vaccines)

IT Toxins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(enterotoxins, heat-labile; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems  
(epidural; weak antigens inserted with foreign T cell epitope as vaccines)

IT Mucins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(episialins; weak antigens inserted with foreign T cell epitope as vaccines)

IT B cell (lymphocyte)  
T cell (lymphocyte)  
(epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Hemagglutinins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Functional groups  
(farnesyl; weak antigens inserted with foreign T cell epitope as vaccines)

IT Receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(folate; weak antigens inserted with foreign T cell epitope as

- vaccines)
- IT Immunoglobulins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fragments; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Vascular endothelial growth factor receptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene KDR; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Functional groups  
(geranyl-geranyl; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Protein motifs  
(glycosylation site; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Glycoproteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gp100; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Glycoproteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gp15; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Sialoglycoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gp75; weak antigens inserted with foreign T cell epitope as vaccines)
- IT T cell (lymphocyte)  
(helper cell, epitope; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Phosphoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hsc 70 (heat-shock cognate, 70,000-mol.-wt.); weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(injections, s.c.; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Mutation  
(insertion; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Interleukin receptors  
Interleukin receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(interleukin 13; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(intracranial; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(intracutaneous; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(intradermal; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Hemolysins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(listeriolysins; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mammaglobin; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(melanoma-assocd., MAGE; weak antigens inserted with foreign T cell

- epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(melanoma-assocd., Melan-A/MART-1; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Transferrins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(melanotransferrins; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Chromosome  
(minichromosomes; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Chemicals  
(modification; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Mucins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mucin 2, 3 and 4; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Functional groups  
(myristyl; weak antigens inserted with foreign T cell epitope as vaccines)
- IT DNA  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(naked; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Mammary gland  
Prostate gland  
(neoplasm; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Microorganism  
(non-pathogenic; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Liquids  
(oils formulation; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(oral; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(p15; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Functional groups  
(palmitoyl; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(parenterals; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Drug delivery systems  
(peritoneal; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Glycolipoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(phosphatidylinositol-contg.; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(probasins; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Glycoproteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prostateins; weak antigens inserted with foreign T cell epitope as vaccines)



IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(self; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems  
(spinal; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems  
(subdermal; weak antigens inserted with foreign T cell epitope as vaccines)

IT Drug delivery systems  
(sublingual; weak antigens inserted with foreign T cell epitope as vaccines)

IT Mutation  
(substitution; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(surface; weak antigens inserted with foreign T cell epitope as vaccines)

IT Genetic element  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(terminator; weak antigens inserted with foreign T cell epitope as vaccines)

IT Toxoids  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tetanus, epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transfection-facilitating; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transmembrane, mesothelin; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., G250; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., GAGE; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., KIAA0205 bladder carcinoma antigen; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., MAP17; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., MIC A/B; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., MUM-1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (tumor-assocd., NY-ESO-1; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., PRAME; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., Pmel-17; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., RCAS1; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., ZAG; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd., p16INK4; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-assocd.; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Antigens  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tumor-rejection, RAGE-1; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Complement receptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type 1; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Complement receptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type 2; weak antigens inserted with foreign T cell epitope as vaccines)
- IT Animal  
Animal cell line  
Antigen-presenting cell  
Antitumor agents  
Bacteriophage  
Carriers  
Cosmids  
DNA sequences  
Dendritic cell  
Encapsulation  
Epitopes  
Immunotherapy  
Influenza virus  
Latex  
Liposomes  
Macrophage  
Micelles  
Molecular cloning  
Mycobacterium  
Particles  
Plasmids  
Plasmodium falciparum

Protein sequences  
 Quillaja saponaria  
 Vaccines  
 Virus  
 Virus vectors  
 (weak antigens inserted with foreign T cell epitope as vaccines)  
 IT Gene, animal  
 Promoter (genetic element)  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (weak antigens inserted with foreign T cell epitope as vaccines)  
 IT CA 125 (carbohydrate antigen)  
 CD19 (antigen)  
 CD20 (antigen)  
 CD22 (antigen)  
 CD44 (antigen)  
 CD45 (antigen)  
 CD5 (antigen)  
 CD59 (antigen)  
 Carcinoembryonic antigen  
 Enzymes, biological studies  
 Epidermal growth factor receptors  
 Haptens  
 .alpha.-Fetoproteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (weak antigens inserted with foreign T cell epitope as vaccines)  
 IT Antibodies  
 Antigens  
 CD40 (antigen)  
 CTLA-4 (antigen)  
 Calreticulin  
 Carbohydrates, biological studies  
 Cytokines  
 DNA  
 Heat-shock proteins  
 Insulin-like growth factor I receptors  
 Interleukin 1  
 Interleukin 12  
 Interleukin 13  
 Interleukin 15  
 Interleukin 2  
 Interleukin 4  
 Interleukin 6  
 Ki-67 antigen  
 Lipid A  
 Lipids, biological studies  
 Osteonectin  
 Plastics, biological studies  
 Platelet-derived growth factors  
 Polymers, biological studies  
 Receptors  
 Saponins  
 Toxins  
 Tumor necrosis factors  
 neu (receptor)  
 p53 (protein)  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (weak antigens inserted with foreign T cell epitope as vaccines)  
 IT Transforming growth factors  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.alpha.-; weak antigens inserted with foreign T cell epitope as  
 vaccines)  
 IT Catenins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transforming growth factors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; weak antigens inserted with foreign T cell epitope as vaccines)

IT Interferons  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.gamma.; weak antigens inserted with foreign T cell epitope as vaccines)

IT 39391-18-9  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(2; weak antigens inserted with foreign T cell epitope as vaccines)

IT 62031-54-3, FGF  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(8a and 8b isoforms; weak antigens inserted with foreign T cell epitope as vaccines)

IT 264178-47-4P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(P2 epitope gene; weak antigens inserted with foreign T cell epitope as vaccines)

IT **126779-13-3P**  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(P2 epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT 264185-70-8P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(P30 epitope gene; weak antigens inserted with foreign T cell epitope as vaccines)

IT **126779-14-4P**  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(P30 epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT 99-20-7D, Trehalose, diester 7429-90-5, Aluminum, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 25322-68-3 53678-77-6, Muramyl dipeptide  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adjuvant; weak antigens inserted with foreign T cell epitope as vaccines)

IT 148997-75-5, Androgen-induced growth factor (mouse clone pSC17 precursor reduced) 264179-58-0 264179-59-1, Neu (receptor) (human) 264179-62-6 264179-64-8 264179-65-9 264179-66-0 264179-67-1 264179-68-2  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(amino acid sequence; weak antigens inserted with foreign T cell epitope as vaccines)

IT 3458-28-4, Mannose 9036-88-8, Mannan  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(binding partner; weak antigens inserted with foreign T cell epitope as vaccines)

IT 56093-23-3  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fusion with LDL receptor; weak antigens inserted with foreign T cell epitope as vaccines)

IT 125978-95-2, Nitric oxide synthase  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inducible; weak antigens inserted with foreign T cell epitope as vaccines)

IT 9030-23-3, Thymidine phosphorylase  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibitor; weak antigens inserted with foreign T cell epitope as vaccines)

IT 141907-41-7, Matrix metalloproteinase  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (isoforms; weak antigens inserted with foreign T cell epitope as vaccines)

IT 100040-73-1, DNA (human clone .lambda.HER2-436 gene HER2 receptor cDNA)  
 264179-57-9 264179-60-4 264179-61-5 264179-63-7  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (nucleotide sequence; weak antigens inserted with foreign T cell epitope as vaccines)

IT 52-90-4, Cysteine, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (residue; weak antigens inserted with foreign T cell epitope as vaccines)

IT 217865-15-1 259127-00-9, 9: PN: US6027895 SEQID: 10 unclaimed DNA  
 264179-74-0 264179-76-2 264179-77-3  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; novel methods for therapeutic vaccination)

IT 179920-34-4  
 RL: PRP (Properties)  
 (unclaimed protein sequence; novel methods for therapeutic vaccination)

IT 64134-30-1 137219-78-4 264134-74-9 264134-75-0 264134-76-1  
 264134-77-2 264179-75-1  
 RL: PRP (Properties)  
 (unclaimed sequence; novel methods for therapeutic vaccination)

IT 264134-70-5P 264134-71-6P 264134-72-7P 264134-73-8P 264134-78-3P  
 264224-61-5P 264224-76-2P  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);  
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (weak antigens inserted with foreign T cell epitope as vaccines)

IT 71965-46-3, Cathepsins 99085-47-9, Complement decay-accelerating factor  
 147014-97-9, Cyclin-dependent kinase 4 179241-78-2, Caspase 8  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (weak antigens inserted with foreign T cell epitope as vaccines)

IT 251541-10-3, Human Her2 protein (59-73) 251542-12-8, Human Her2 protein  
 (465-479) 264617-99-4, Human PSM (87-108) 264618-03-3, Human PSM  
 (210-230) 264618-06-6, Human PSM (269-289) 264618-07-7, Human PSM  
 (298-324) 264618-08-8, Human PSM (442-465) 264618-09-9, Human PSM  
 (488-514) 264618-23-7, Human PSM (598-630) 264619-18-3, Human PSM  
 (643-662) 264619-84-3, Human PSM (672-699) 264620-57-7, Human Her2  
 protein (5-25) 264620-84-0, Human Her2 protein (103-117) 264621-04-7,  
 Human Her2 protein (149-163) 264621-94-5, Human Her2 protein (210-224)  
 264622-06-2, Human Her2 protein (250-264) 264622-08-4, Human Her2  
 protein (325-339) 264622-09-5, Human Her2 protein (369-383)  
 264622-23-3, Human Her2 protein (579-593) 264624-69-3, Human Her2  
 protein (632-652) 264624-79-5, Human Her2 protein (653-667)  
 264624-80-8, Human Her2 protein (661-675) 264625-23-2, Human Her2  
 protein (695-709) 264625-25-4, Human Her2 protein (72-86) 264625-36-7,

Human Her2 protein (146-160) 264625-37-8, Human Her2 protein (221-235)  
264625-38-9, Human Her2 protein (257-271) 264625-51-6, Human FGF8b  
protein (1-54) 264626-02-0, Human FGF8b protein (55-58) 264626-17-7,  
Human FGF8b protein (178-215) 264626-69-9, Human FGF8b protein (63-68)  
264626-82-6, Human FGF8b protein (72-76) 264626-84-8, Human FGF8b  
protein (85-91) 264626-85-9, Human FGF8b protein (95-102) 264626-86-0,  
Human FGF8b protein (106-111) 264626-87-1, Human FGF8b protein (115-120)  
264627-05-6, Human FGF8b protein (128-134) 264627-07-8, Human FGF8b  
protein (138-144) 264627-09-0, Human FGF8b protein (149-154)  
264627-10-3, Human FGF8b protein (158-162) 264627-11-4, Human FGF8b  
protein (173-177) 264627-12-5, Human FGF8b protein (26-45)  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(weak antigens inserted with foreign T cell epitope as vaccines)  
IT 3700-67-2 9001-91-6, Plasminogen 9002-10-2, Tyrosinase 9002-61-3,  
Human chorionic gonadotropin 9032-22-8, Mox1 oxidase 9034-40-6,  
Gonadotropin-releasing hormone 9081-34-9, 5.alpha. Reductase  
50812-37-8, Glutathione S-transferase 60748-06-3, Gastrin 17  
62010-37-1, GD3 65988-71-8, GD2 66456-69-7, GM4 66594-14-7, Quil A  
80043-53-4, Gastrin-releasing peptide 83588-90-3, N-  
Acetylglucosaminyltransferase V 83869-56-1, GM-CSF 89800-66-8,  
Heparanase 120178-12-3, Telomerase 127464-60-2, Vascular endothelial  
growth factor 140208-23-7, Plasminogen activator inhibitor-1  
141256-04-4, QS21

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(weak antigens inserted with foreign T cell epitope as vaccines)  
IT 61512-21-8, Thymosin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta. 15; weak antigens inserted with foreign T cell epitope as  
vaccines)

IT 9005-80-5, Inulin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.gamma.-; weak antigens inserted with foreign T cell epitope as  
vaccines)

L58 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:191227 HCAPLUS

DN 132:235902

TI Down-regulating osteoprotegerin ligand activity with  
autovaccines

IN **Halkier, Torben**; Haaning, Jesper

PA M & E Biotech A/S, Den.

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-62

ICS C12N015-86; C12N015-12; C12N005-10; C12N001-21; C12N001-19;  
C07K014-705; A61K039-00; A61K031-713; G01N033-50

CC 15-2 (Immunochemistry)

Section cross-reference(s): 3

FAN.CNT 1

|    | PATENT NO.    | KIND  | DATE     | APPLICATION NO. | DATE         |
|----|---------------|---|----------|-----------------|--------------|
|    | -----         | ----  | -----    | -----           | -----        |
| PI | WO 2000015807 | A1  | 20000323 | WO 1999-DK481   | 19990913 <-- |
|    | W:            | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,     |          |                 |              |
|    |               | CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE,                     |          |                 |              |
|    |               | GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, |          |                 |              |
|    |               | LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, |          |                 |              |
|    |               | RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,     |          |                 |              |
|    |               | VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM              |          |                 |              |
|    | RW:           | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, |          |                 |              |
|    |               | ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, |          |                 |              |



CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

|            |    |          |                 |              |
|------------|----|----------|-----------------|--------------|
| CA 2343654 | AA | 20000323 | CA 1999-2343654 | 19990913 <-- |
| AU 9956173 | A1 | 20000403 | AU 1999-56173   | 19990913 <-- |
| EP 1114166 | A1 | 20010711 | EP 1999-942778  | 19990913 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE,  
SI, LT, LV, FI, RO

|               |    |          |                |              |
|---------------|----|----------|----------------|--------------|
| JP 2002525060 | T2 | 20020813 | JP 2000-570334 | 19990913 <-- |
| NO 2001001304 | A  | 20010515 | NO 2001-1304   | 20010314 <-- |

PRAI DK 1998-1164 A 19980915 <--  
US 1998-102896P P 19981002 <--  
WO 1999-DK481 W 19990913 <--

AB The invention provides a novel method for down-**regulating** the biol. activity of osteoprotegerin ligand (OPGL, also known as TRANCE) thereby rendering possible the treatment/amelioration of diseases characterized by excessive loss of bone mass, e.g. osteoporosis. Down-**regulation** is effected by inducing an immune response against OPGL in an individual in need thereof. Immune responses can be raised by classical immunization with immunogenic variants of OPGL or by nucleic acid immunization where the nucleic acids encode the OPGL variant. Immunogenic compns. are constructed comprising residues 158-316 of murine OPGL fused to His tags, for ease of purifn., and, optionally, contg. inserted T cell epitope peptides from tetanus toxoid (P2 or P30 epitopes), diphtheria toxoid, influenza virus hemagglutinin, or plasmodium falciparum circumsporozoite protein. The invention pertains to compns., polypeptides and nucleic acids useful in the invention, as well as to vectors and transformed host cells useful in the prepn. thereof.

ST osteoprotegerin ligand **downregulation** vaccine; sequence  
osteoprotegerin ligand cDNA mouse human; immunization osteoprotegerin ligand nucleic acid; osteoporosis treatment osteoprotegerin ligand autovaccine

IT Antigens  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(CS (circumsporozoite), T cell epitopes fusion products with Plasmodium falciparum; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT Heat-shock proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HSP 70, co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT Heat-shock proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HSP 90, co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT Hemagglutinins  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(T cell epitopes fusion products with influenza virus hemagglutinin; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT Lymph node  
(artificial; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT Calreticulin  
Cytokines  
Heat-shock proteins  
Hormones, animal, biological studies  
Interleukin 12  
Interleukin 13  
Interleukin 15  
Interleukin 4  
Interleukin 6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Toxoids  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(diphtheria, T cell epitopes fusion products; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Cosmids  
DNA sequences  
Plasmid vectors  
Protein sequences  
Vaccines  
Virus vectors  
(down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Synthetic gene  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Glycophosphoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(endoplasmic, co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT cDNA sequences  
(for murine and human osteoprotegerin ligands; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Phosphoproteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hsc 70 (heat-shock cognate, 70,000-mol.-wt.), co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Animal cell  
(insect, transformed; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Animal cell  
(mammalian, transformed; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Chromosome  
(minichromosomes, vectors; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Immunization  
(nucleic acid; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Bone  
(resorption, treatment of excess; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Toxoids  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(tetanus, T cell epitopes fusion products; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Osteoporosis  
(therapeutic agents; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Bacteria (Eubacteria)  
Fungi  
Plant cell  
Protozoa  
Yeast  
(transformed; down-**regulating** osteoprotegerin ligand activity with autovaccines)
- IT Bacteriophage  
(vectors; down-**regulating** osteoprotegerin ligand activity

with autovaccines)

IT Interferons  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.gamma., co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 261754-98-7P 261755-01-5P 261755-03-7P 261755-08-2P 261755-10-6P  
261755-12-8P 261755-14-0P  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 198086-51-0, GenBank AB008426-derived protein GI 3041782 200145-93-3  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 83869-56-1, Granulocyte-macrophage colony stimulating factor  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-expression of; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 207621-35-0P, Osteoclast differentiation factor  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 261754-99-8P 261755-00-4P 261755-02-6P 261755-07-1P 261755-09-3P  
261755-11-7P 261755-13-9P  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(nucleotide sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 206615-21-6, GenBank AB008426 206826-73-5 206826-74-6, GenBank AF053713  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 261755-22-0 261755-23-1 261755-24-2 261755-25-3 261755-26-4  
261755-27-5 261755-28-6 261755-29-7 261755-30-0 261755-31-1  
261755-32-2 261755-33-3 261755-34-4  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

IT 126779-13-3 126779-14-4  
RL: PRP (Properties)  
(unclaimed protein sequence; down-**regulating** osteoprotegerin ligand activity with autovaccines)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Amgen Inc; WO 9723614 A 1997 HCAPLUS
- (2) Amgen Inc; WO 9846751 A 1998 HCAPLUS
- (3) Fuller, K; J EXP MED 1998, V188(5), P997 HCAPLUS
- (4) Immunex Corp; WO 9828426 A 1998 HCAPLUS
- (5) Schering Corp; WO 9825958 A 1998 HCAPLUS
- (6) Univ Columbia; WO 9720063 A 1997 HCAPLUS
- (7) Univ Utah; WO 9527058 A 1995 HCAPLUS

L58 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:68486 HCAPLUS

DN 132:118343

TI Growth differentiation factor GDF-

8 promoter and its uses for tissue-specific gene expression and identification of GDF expression regulators

IN Liang, Li-Fang  
 PA Metamorphix, Inc., USA  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-00  
 CC 3-2 (Biochemical Genetics)  
 Section cross-reference(s): 2, 13

FAN.CNT 1

|      | PATENT NO.   | KIND   | DATE     | APPLICATION NO. | DATE         |
|------|--|--|----------|-----------------|--------------|
| PI   | WO 2000004051  | A2   | 20000127 | WO 1999-US16026 | 19990715 <-- |
|      | WO 2000004051  | A3   | 20000525 |                 |              |
|      | W:   | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |              |
|      | RW:  | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |              |
|      | CA 2333465   | AA   | 20000127 | CA 1999-2333465 | 19990715 <-- |
|      | AU 9955427   | A1   | 20000207 | AU 1999-55427   | 19990715 <-- |
|      | EP 1097233   | A2   | 20010509 | EP 1999-941954  | 19990715 <-- |
|      | R:   | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |          |                 |              |
|      | JP 2002520043  | T2   | 20020709 | JP 2000-560157  | 19990715 <-- |
| PRAI | US 1998-92865P   | P  | 19980715 | <--             |              |
|      | US 1999-123270P  | P  | 19990308 | <--             |              |
|      | WO 1999-US16026  | W  | 19990715 | <--             |              |
| AB   | The complete nucleotide sequences of <b>GDF</b> promoters (e.g., <b>GDF-8</b> promoters) from human, mouse, chicken, and pig are described. Also described are methods of using the <b>GDF</b> promoters to <b>regulate</b> tissue-specific, particularly <b>muscle</b> -specific gene expression, and to identify compds. which <b>regulate</b> <b>GDF</b> expression. Expression vector constructs comprising the <b>GDF-8</b> gene promoter fused to a gene of interest, possibly a reporter gene are provided. |  |          |                 |              |
| ST   | tissue specific gene expression <b>GDF regulator</b> ; sequence growth differentiation factor <b>GDF8</b> promoter human chicken pig   |  |          |                 |              |
| IT   | Gene<br>(expression, <b>muscle</b> -specific; <b>growth differentiation factor GDF-8</b> promoter and uses for tissue-specific gene expression and identification of <b>GDF</b> expression <b>regulators</b> )   |  |          |                 |              |
| IT   | Chicken ( <i>Gallus domesticus</i> )<br>Mouse ( <i>Mus musculus</i> )<br>Swine<br>( <b>growth differentiation factor GDF-8</b> promoter and uses for tissue-specific gene expression and identification of <b>GDF</b> expression <b>regulators</b> )   |  |          |                 |              |
| IT   | Growth factors, animal<br>RL: BSU (Biological study, unclassified); BIOL (Biological study)<br>( <b>growth differentiation factor GDF-8</b> promoter and uses for tissue-specific gene expression and identification of <b>GDF</b> expression <b>regulators</b> )  |  |          |                 |              |
| IT   | Reporter gene<br>RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  |  |          |                 |              |

- (**growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Drug delivery systems  
(**injections, of GDF promoter into a muscle cell or transgenic animal; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Transformation, genetic  
(**microinjection; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Growth factors, animal  
Growth inhibitors, animal  
RL: ANT (Analyte); ANST (Analytical study)  
(**of GDF expression; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Promoter (genetic element)  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)  
(**of growth differentiation factor GDF-8 gene; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT DNA sequences  
(**of growth differentiation factor GDF-8 promoter; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Genetic vectors  
(**pGL3-0.65; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT Muscle  
(**transfection of; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT 256216-14-5P 256216-15-6P 256216-16-7P  
256216-17-8P 256216-18-9P 256216-19-0P  
256216-20-3P 256216-21-4P  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)  
(**nucleotide sequence; growth differentiation factor GDF-8 promoter and uses for tissue-specific gene expression and identification of GDF expression regulators**)
- IT 256216-88-3, 3: PN: WO0004051 SEQID: 3 unclaimed DNA  
RL: PRP (Properties)  
(**unclaimed nucleotide sequence; growth differentiation factor GDF-8**)

promoter and its uses for tissue-specific gene expression and identification of **GDF** expression **regulators**)

L58 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:741730 HCAPLUS

DN 131:321960

TI Anti-**myostatin** vaccine for increasing **muscle** mass in animals

IN Hickey, Gerard F.

PA Merck and Co., Inc., USA

SO Brit. UK Pat. Appl., 10 pp.

CODEN: BAXXDU

DT Patent

LA English

IC ICM A61K039-395

ICS A61K039-385

ICA C07K014-495

CC 18-6 (Animal Nutrition)

Section cross-reference(s): 15, 63

FAN.CNT 1

|      | PATENT NO.     | KIND | DATE         | APPLICATION NO. | DATE         |
|------|----------------|------|--------------|-----------------|--------------|
| PI   | GB 2333706     | A1   | 19990804     | GB 1999-2041    | 19990129 <-- |
| PRAI | US 1998-73438P | P    | 19980202 <-- |                 |              |

AB A method for increasing the **muscle** mass in animals, such as cow, sheep, pig, and chicken, comprises (a) administering a **vaccine** which will promote the prodn. of anti-**myostatin** (i.e., anti-**growth differentiation factor 8** or **GDF-8**) antibodies, or (b) providing the animal with an immunoneutralizing amt. of anti-**myostatin** antibodies. **Myostatin**, a member of the transforming growth factor (TGF) superfamily of proteins, is thought to exert a neg. control on the amt. of skeletal **muscle** mass in an animal. The use of a **vaccine** or antibodies to **myostatin** allows one to increase the skeletal **muscle** mass in domesticated animals and thus increase their value as food sources. The **vaccine** may be a hapten-carrier protein conjugate in which the hapten is an epitope of **myostatin**, particularly from the functional domain at the C-terminus, or it may be a fusion protein comprising such an epitope fused to a carrier protein. The fusion protein product is obtained using std. **recombinant** DNA procedures using *E. coli* as host. The **vaccine** is preferably administered in a formulation also contg. an adjuvant such as an aluminum salt (AlPO<sub>4</sub>) or an oil-in-water emulsion such as vitamin E acetate solubilizate. Immunoneutralization of **myostatin** may occur after a single dose or a once-yearly dose may be applied. Immunoneutralization may also be induced in pregnant animals resulting in transplacental transfer of anti-**myostatin** antibodies to the fetus and consequent increased **muscle** mass in the offspring.

ST **muscle** mass enhancer antibody **myostatin** immunoneutralization

IT Anabolic agents

**Muscle**

**Vaccines**

(anti-**myostatin** vaccine for increasing **muscle** mass in animals)

IT Proteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**myostatin**, antibodies specific for; anti-**myostatin**

**vaccine** for increasing **muscle** mass in animals)

IT Antibodies

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study);



PREP (Preparation); PROC (Process); USES (Uses)  
 (myostatin-specific; anti-myostatin vaccine  
 for increasing muscle mass in animals)

IT Meat  
 (prodn. of; anti-myostatin vaccine for increasing  
 muscle mass in animals)

L58 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1999:549369 HCAPLUS  
 DN 131:198614  
 TI Immunological methods to modulate myostatin in vertebrate  
 subjects  
 IN Barker, Christopher A.; Morsey, Mohamad  
 PA Biostar Inc., Can.  
 SO PCT Int. Appl., 109 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C12N015-12  
 ICS C12N015-62; C12N005-10; C07K014-475; C07K016-22; A61K038-17  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 2, 5, 14

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE         | APPLICATION NO. | DATE         |
|------|---|------|--------------|-----------------|--------------|
| PI   | WO 9942573  | A1   | 19990826     | WO 1999-CA128   | 19990219 <-- |
|      | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |              |                 |              |
|      | US 6369201  | B1   | 20020409     | US 1999-252149  | 19990218 <-- |
|      | ZA 9901369  | A    | 19990820     | ZA 1999-1369    | 19990219 <-- |
|      | CA 2323607  | AA   | 19990826     | CA 1999-2323607 | 19990219 <-- |
|      | AU 9925073  | A1   | 19990906     | AU 1999-25073   | 19990219 <-- |
|      | EP 1056845  | A1   | 20001206     | EP 1999-904660  | 19990219 <-- |
|      | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |              |                 |              |
|      | BR 9907995  | A    | 20010515     | BR 1999-7995    | 19990219 <-- |
|      | JP 2002504326   | T2   | 20020212     | JP 2000-532513  | 19990219 <-- |
| PRAI | US 1998-75213P  | P    | 19980219 <-- |                 |              |
|      | WO 1999-CA128   | W    | 19990219 <-- |                 |              |

AB Immunol. compns. and methods for reducing myostatin activity in vertebrate subjects are disclosed. The compns. include myostatin peptide immunogens, myostatin multimers and/or myostatin immunoconjugates capable of eliciting an immune response in a vertebrate subject to which the compns. are administered. The methods are useful for modulating endogenous myostatin activity in vertebrate and are also useful for treating a wide variety of disorders that cause degeneration or wasting of muscle.

ST myostatin immunoconjugate vaccine vertebrate muscle degeneration

IT Immunostimulants  
 (adjuvants; compn. comprising peptide or multimer or immunoconjugate of myostatin for modulating endogenous myostatin and for treating muscle wasting)

IT Epitopes  
 Livestock  
 Molecular cloning  
 Protein sequences

**Vaccines**

Vertebrate (Vertebrata)

(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Antibodies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT **Muscle**, disease

(degeneration; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Growth factors, animal

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(growth differentiation factor 11; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT T cell (lymphocyte)

(helper cell, epitope; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Drug delivery systems

(immunoconjugates; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Appetite

Body weight

Lactation

Longevity

Mammary gland

(increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Toxins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(leukotoxins, **myostatin** conjugate; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT **Muscle**

(mass and strength increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Growth factors, animal

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**myostatin**; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Adipose tissue

(redn.; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT Feed

(uptake increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

IT **Muscle**, disease

(wasting; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for

treating muscle wasting)

IT 161135-84-8 161135-86-0 199810-43-0,  
 Myostatin (chicken muscle gene MSTN) 199810-45-2  
 , Myostatin (swine muscle gene MSTN)  
 240485-48-7, Myostatin (swine) 240485-51-2,  
 Myostatin (sheep) 240485-53-4, Myostatin  
 (chicken) 240485-55-6, Myostatin (turkey)  
 240485-57-8, Myostatin (zebra fish) 240485-59-0  
 , 45-376-Myostatin (mouse) 240485-61-4, 45-376-  
 Myostatin (rat) 240485-63-6, 45-375-Myostatin  
 (human clone 3) 240485-65-8, 45-375-Myostatin (baboon)  
 240485-67-0, 45-375-Myostatin (cattle clone 5)  
 240485-69-2, 45-375-Myostatin (swine)  
 240485-70-5, 45-375-Myostatin (sheep)  
 240485-72-7, 45-375-Myostatin (chicken)  
 240485-73-8, 45-375-Myostatin (turkey)  
 240485-75-0, 45-374-Myostatin (zebra fish)  
 240486-08-2, Myostatin (cattle clone 5)  
 240486-09-3, 235-376-Myostatin (mouse)  
 240486-14-0, 235-375-Myostatin (human clone 3)  
 240486-21-9, 235-375-Myostatin (baboon)  
 240486-26-4, 235-375-Myostatin (cattle clone 5)  
 240486-35-5, 235-375-Myostatin (sheep)  
 240486-37-7, 235-375-Myostatin (chicken)  
 240486-42-4, 235-375-Myostatin (turkey)  
 240486-46-8, 235-374-Myostatin (zebra fish)  
 240486-50-4, 1-350-Myostatin (mouse) 240486-52-6  
 , 1-350-Myostatin (rat) 240486-53-7, 1-350-  
 Myostatin (human clone 3) 240486-54-8, 1-350-  
 Myostatin (baboon) 240486-55-9, 1-350-Myostatin  
 (cattle clone 5) 240486-56-0, 1-350-Myostatin (swine)  
 240486-57-1, 1-350-Myostatin (sheep) 240486-58-2  
 , 1-350-Myostatin (chicken) 240486-59-3, 1-350-  
 Myostatin (turkey) 240486-60-6, 1-350-Myostatin  
 (zebra fish) 240486-61-7, 1-275-Myostatin (mouse)  
 240486-63-9, 1-275-Myostatin (rat) 240486-64-0  
 , 1-275-Myostatin (human clone 3) 240486-65-1, 1-275-  
 Myostatin (baboon) 240486-66-2, 1-275-Myostatin  
 (cattle clone 5) 240486-67-3, 1-275-Myostatin (swine)  
 240486-68-4, 1-275-Myostatin (sheep) 240486-69-5  
 , 1-275-Myostatin (chicken) 240486-70-8, 1-275-  
 Myostatin (turkey) 240486-71-9, 1-275-Myostatin  
 (zebra fish) 240486-72-0, 25-300-Myostatin (mouse)  
 240486-73-1, 25-300-Myostatin (rat) 240486-74-2  
 , 25-300-Myostatin (human clone 3) 240486-76-4,  
 25-300-Myostatin (baboon) 240486-77-5, 25-300-  
 Myostatin (cattle clone 5) 240486-78-6, 25-300-  
 Myostatin (swine) 240486-79-7, 25-300-Myostatin  
 (sheep) 240486-80-0, 25-300-Myostatin (chicken)  
 240486-81-1, 25-300-Myostatin (turkey)  
 240486-82-2, 25-300-Myostatin (zebra fish)  
 240486-83-3, 50-325-Myostatin (mouse)  
 240486-90-2, 50-325-Myostatin (rat) 240486-91-3  
 , 50-325-Myostatin (human clone 3) 240486-95-7,  
 50-325-Myostatin (baboon) 240486-96-8, 50-325-  
 Myostatin (cattle clone 5) 240486-98-0, 50-325-  
 Myostatin (swine) 240486-99-1, 50-325-Myostatin  
 (sheep) 240487-00-7, 50-325-Myostatin (chicken)  
 240487-01-8, 50-325-Myostatin (turkey)  
 240487-02-9, 50-325-Myostatin (zebra fish)  
 240487-03-0, 75-350-Myostatin (mouse)  
 240487-04-1, 75-350-Myostatin (rat) 240487-05-2  
 , 75-350-Myostatin (human clone 3) 240487-06-3,

75-350-Myostatin (baboon) 240487-07-4, 75-350-Myostatin (cattle clone 5) 240487-08-5, 75-350-Myostatin (swine) 240487-09-6, 75-350-Myostatin (sheep) 240487-10-9, 75-350-Myostatin (chicken) 240487-11-0, 75-350-Myostatin (turkey) 240487-12-1, 75-350-Myostatin (zebra fish) 240487-14-3, 100-376-Myostatin (mouse) 240487-15-4, 100-376-Myostatin (rat) 240487-16-5, 100-375-Myostatin (human clone 3) 240487-17-6, 100-375-Myostatin (baboon) 240487-18-7, 100-375-Myostatin (cattle clone 5) 240487-19-8, 100-375-Myostatin (swine) 240487-20-1, 100-375-Myostatin (sheep) 240487-21-2, 100-375-Myostatin (chicken) 240487-22-3, 100-375-Myostatin (turkey) 240487-23-4, 100-374-Myostatin (zebra fish)

RL: PRP (Properties)

(amino acid sequence; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

|    |             |             |             |             |             |
|----|-------------|-------------|-------------|-------------|-------------|
| IT | 240123-41-5 | 240123-42-6 | 240123-43-7 | 240123-44-8 | 240123-45-9 |
|    | 240123-46-0 | 240123-47-1 | 240123-48-2 | 240123-49-3 | 240123-50-6 |
|    | 240123-51-7 | 240123-52-8 | 240123-53-9 | 240123-54-0 | 240123-55-1 |
|    | 240123-56-2 | 240123-57-3 | 240123-58-4 | 240123-59-5 | 240123-60-8 |
|    | 240123-61-9 | 240123-62-0 | 240123-63-1 |             |             |

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating **muscle** wasting)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Kambadur; GENOME RESEARCH 1997, V7(9), P910 HCAPLUS
- (2) McPherron And Lee; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1997, V94(23), P12457
- (3) Michel, G; WO 9902667 A 1999 HCAPLUS
- (4) Univ Johns Hopkins Med; WO 9421681 A 1994 HCAPLUS
- (5) Univ Johns Hopkins Med; WO 9601845 A 1996 HCAPLUS
- (6) Univ Johns Hopkins Med; WO 9833887 A 1998 HCAPLUS

L58 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:506168 HCAPLUS

DN 131:282112

TI PCR based detection of bovine **myostatin** Q204X **mutation**

AU Antoniou, E.; Grosz, M.

CS Fort Keogh Livestock and Range Research Laboratory, Miles City, MT, 59301, USA

SO Animal Genetics (1999), 30(3), 231-232

CODEN: ANGE3; ISSN: 0268-9146

PB Blackwell Science Ltd.

DT Journal

LA English

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 2, 13

AB The bovine **myostatin** gene GDF8 is responsible for the double-**muscled** phenotype obsd. in the Charolais breed. The mutant allele contains a T instead of a C at nucleotide position 610 from the start codon. A PCR based test was designed to differentiate between the normal and mutant alleles.

ST PCR detection cattle **myostatin** gene GDF8 **mutation**

IT Gene, animal

RL: BSU (Biological study, unclassified); BIOL (Biological study) (GDF8; PCR based detection of bovine **myostatin** Q204X **mutation**)

IT Alleles  
Cattle  
PCR (polymerase chain reaction)  
(PCR based detection of bovine **myostatin** Q204X  
**mutation**)

IT Primers (nucleic acid)  
RL: AGR (Agricultural use); ARG (Analytical reagent use); BUU (Biological  
use, unclassified); ANST (Analytical study); BIOL (Biological study); USES  
(Uses)  
(PCR based detection of bovine **myostatin** Q204X  
**mutation**)

IT Growth factors, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**myostatin**; PCR based detection of bovine **myostatin**  
Q204X **mutation**)

IT **Mutation**  
(**point**, Q204X; PCR based detection of bovine  
**myostatin** Q204X **mutation**)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Liu; Genes Dev 1997, V11, P179 HCAPLUS  
(2) McCracken; Anim Genet 1997, V28, P459 HCAPLUS

L58 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:375567 HCAPLUS

DN 131:28319

TI Maintenance of vascular smooth **muscle** integrity by morphogenic  
**proteins**

IN Nakaoka, Takashi; Miyazono, Kohei; Sampath, Kuber T.

PA Creative Biomolecules, Inc., USA

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-00

CC 2-10 (Mammalian Hormones)

Section cross-reference(s): 1, 63

FAN.CNT 1

|    | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|----|--|------|----------|-----------------|--------------|
| PI | WO 9928341   | A2   | 19990610 | WO 1998-US25398 | 19981130 <-- |
|    | WO 9928341   | A3   | 19990805 |                 |              |
|    | W: AU, CA, JP, US  |      |          |                 |              |
|    | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |              |
|    | CA 2314423   | AA   | 19990610 | CA 1998-2314423 | 19981130 <-- |
|    | AU 9917064   | A1   | 19990616 | AU 1999-17064   | 19981130 <-- |
|    | EP 1037910   | A2   | 20000927 | EP 1998-961838  | 19981130 <-- |
|    | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI  |      |          |                 |              |

PRAI US 1997-67690P P 19971204 <--

WO 1998-US25398 W 19981130 <--

AB Disclosed are compns. and methods for maintaining the integrity of smooth **muscle**, particularly vascular smooth **muscle**. Vascular diseases are characterized by an excessive build-up of vascular smooth **muscle** cells, resulting in an occlusion of a blood vessel, and/or by loss of elasticity in the blood vessels. Causes of blood vessel occlusion include smooth **muscle** cell proliferation and inflammatory responses. Inhibition of the proliferation of smooth **muscle** cells or inflammatory responses represents an effective treatment for vascular disorders, such as atherosclerosis and restenosis. Treatment may include administration of a morphogenic **protein**. The **protein** itself may be delivered to the site of vascular



occlusion or the **protein** may be delivered by a vector, such as an adenoviral vector contg. a DNA **insert** encoding a morphogenic **protein**. Such compns. and methods may also inhibit the responses of smooth **muscle** cells to various traumas, such as exposure to toxic agents. All of these treatments operate to preserve the cell phenotype by inhibiting an increase in extracellular matrix **proteins**, such as collagen, or by maintaining the normal balance of extracellular matrix **proteins**, such as Types I and III collagen.

ST morphogenic **protein** vascular smooth **muscle** proliferation

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(3; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(4; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(5; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(6; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(6A; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT Bone morphogenetic **proteins**

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(7; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(BMP-10 (bone morphogenetic **protein** 10); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)



- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-11 (bone morphogenetic **protein** 11); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-12 (bone morphogenetic **protein** 12); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-15 (bone morphogenetic **protein** 15); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-16 (bone morphogenetic **protein** 16); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-9 (bone morphogenetic **protein** 9); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Enhancer (genetic element)  
RL: PEP (Physical, engineering or chemical process); PROC (Process)  
(CMV-IE; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DPP; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-1 (growth/differentiation factor 1); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-10 (growth/differentiation factor 10); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-11 (growth/differentiation factor 11); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

- (GDF-3 (growth/differentiation factor 3); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-5 (growth/differentiation factor 5); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-6 (growth/differentiation factor 6); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-7 (growth/differentiation factor 7); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-8 (growth/differentiation factor 8); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Growth factors, animal  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(GDF-9 (growth/differentiation factor 9); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Cytomegalovirus  
(IE enhancer of; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(OP-2 (osteogenic **protein** 2); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(OP-3 (osteogenic **protein** 3); maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Vgl; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Proteins**, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Vgr; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Medical equipment  
(angioplasty devices, morphogen adsorption on; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Artery  
(angioplasty, restenosis after; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Antiarteriosclerotics  
(antiatherosclerotics; maintenance of vascular smooth **muscle**

- integrity with morphogenic **proteins**)
- IT Blood vessel  
(endothelium, inflammation; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Cell proliferation  
Cytotoxic agents  
Gene therapy  
Genetic vectors  
Molecular cloning  
**Protein** sequences  
Transformation, genetic  
Virus vectors  
cDNA sequences  
(maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Promoter (genetic element)  
RL: PEP (Physical, engineering or chemical process); PROC (Process)  
(maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Hormones, animal, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(morphogens; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Adsorption  
(of morphogens on angioplasty equipment; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Proliferation inhibition  
(proliferation inhibitors; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Artery, disease  
(restenosis; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Blood vessel  
(smooth **muscle**; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT **Mutation**  
(**substitution**; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Collagens, biological studies  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)  
(type I, **regulation** of; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Collagens, biological studies  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)  
(type III, **regulation** of; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Adenoviridae  
(vectors; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT Actins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(.beta.-, chicken gene encoding, promoter of; maintenance of vascular smooth **muscle** integrity with morphogenic **proteins**)
- IT 167616-23-1P, Bone morphogenetic **protein** 7 (human)  
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological

study); OCCU (Occurrence); PREP (Preparation); USES (Uses)  
 (amino acid sequence; maintenance of vascular smooth **muscle**  
 integrity with morphogenic **proteins**)

IT 138674-79-0P, DNA (human bone morphogenetic **protein 7** cDNA plus  
 flanks)  
 RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU  
 (Biological study, unclassified); PRP (Properties); BIOL (Biological  
 study); OCCU (Occurrence); PREP (Preparation)  
 (nucleotide sequence; maintenance of vascular smooth **muscle**  
 integrity with morphogenic **proteins**)

L58 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1999:364318 HCAPLUS  
 DN 131:142902  
 TI **Myostatin**, a transforming growth factor-.beta. superfamily  
 member, is expressed in heart **muscle** and is **upregulated**  
 in cardiomyocytes after infarct

AU Sharma, Mridula; Kambadur, Ravi; Matthews, Kenneth G.; Somers, Wayne G.;  
 Devlin, Gerard P.; Conaglen, John V.; Fowke, Peter J.; Bass, John J.  
 CS Growth Physiology, AgResearch, Hamilton, N. Z.  
 SO Journal of Cellular Physiology (1999), 180(1), 1-9  
 CODEN: JCLLAX; ISSN: 0021-9541  
 PB Wiley-Liss, Inc.  
 DT Journal  
 LA English  
 CC 14-5 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 2, 3, 13

AB **Myostatin** is a secreted growth and differentiating factor ( **GDF-8**) that belongs to the transforming growth  
 factor-beta (TGF-.beta.) superfamily. Targeted disruption of the  
**myostatin** gene in mice and a **mutation** in the third exon  
 of the **myostatin** gene in double-**muscl**ed Belgian Blue  
 cattle breed result in skeletal **muscle** hyperplasia. Hence,  
**myostatin** has been shown to be involved in the **regulation**  
 of skeletal **muscle** mass in both mice and cattle. Previous  
 published reports utilizing Northern hybridization had shown that  
**myostatin** expression was seen exclusively in skeletal  
**muscle**. A significantly lower level of **myostatin** mRNA  
 was also reported in adipose tissue. Using a sensitive reverse  
 transcription-polymerase chain reaction (RT-PCR) technique and Western  
 blotting with anti-**myostatin** antibodies, the authors show that  
**myostatin** mRNA and **protein** are not restricted to  
 skeletal **muscle**. The authors also show that **myostatin**  
 expression is detected in the **muscle** of both fetal and adult  
 hearts. Sequence anal. reveals that the Belgian Blue heart  
**myostatin** cDNA sequence contains an 11 nucleotide **deletion**  
 in the third exon that causes a frameshift that eliminates virtually all  
 of the mature, active region of the **protein**. Anti-  
**myostatin** immunostaining on heart sections also demonstrates that  
**myostatin protein** is localized in Purkinje fibers and  
 cardiomyocytes in heart tissue. Furthermore, following myocardial  
 infarction, **myostatin** expression is **upregulated** in the  
 cardiomyocytes surrounding the infarct area. Given that **myostatin**  
 is expressed in fetal and adult hearts and that **myostatin**  
 expression is **upregulated** in cardiomyocytes after the  
 infarction, **myostatin** could play an important role in cardiac  
 development and physiol.

ST **myostatin** expression heart infarction **mutation** Belgian  
 Blue cattle

IT Cattle  
 (Belgian Blue; **myostatin protein** and mRNA  
 expression in fetal and adult heart and skeletal **muscle**,  
**upregulation** in cardiomyocytes after infarct, and

- deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Heart  
(Purkinje fiber; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Transcriptional **regulation**  
(activation; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT **Mutation**  
(**deletion**; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Gene  
(expression; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Embryo, animal  
(fetus; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT **Protein sequences**  
(for **myostatin** of Belgian Blue cattle heart)
- IT Heart, disease  
(infarction; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Heart  
(myocyte; **myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Heart  
**Muscle**  
(**myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT mRNA  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(**myostatin protein** and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation in heart myostatin in Belgian Blue cattle)**
- IT Gene, animal  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)



(**myostatin** protein and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation** in heart **myostatin** in Belgian Blue cattle)

IT Growth factors, animal

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(**myostatin**; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal **muscle**, **upregulation** in cardiomyocytes after infarct, and **deletion mutation** in heart **myostatin** in Belgian Blue cattle)

IT cDNA sequences

(of **myostatin** of Belgian Blue cattle heart)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Birdsall, H; Circulation 1997, V95, P684 HCAPLUS
- (2) Boccard, R; Developments in meat science 1981, V2, P1
- (3) Brand, T; J Mol Cell Cardiol 1995, V27, P5 HCAPLUS
- (4) Engelmann, G; Mech Dev 1992, V38, P85 HCAPLUS
- (5) Grobet, L; Nat Genet 1997, V1, P71
- (6) Hanset, R; Cross-breeding experiments and strategy of beef utilisation to increase beef production 1977, P399
- (7) Harlow, E; Antibodies: a laboratory manual 1988, P283
- (8) Kambadur, R; Genome Res 1997, V7, P910 HCAPLUS
- (9) Kingsley, D; Genes Dev 1994, V8, P133 HCAPLUS
- (10) MacLellan, W; Circ Res 1993, V73, P783 HCAPLUS
- (11) McPherron, A; Growth Factors Cytokines Health Dis 1996, V1B, P357 HCAPLUS
- (12) McPherron, A; Nature 1997, V387, P83 HCAPLUS
- (13) McPherron, A; Proc Natl Acad Sci USA 1997, V94, P12457 HCAPLUS
- (14) Millan, F; Development 1991, V111, P131 HCAPLUS
- (15) Pelton, R; J Cell Biol 1991, V115, P1091 HCAPLUS
- (16) Pott, J; Proc Natl Acad Sci USA 1991, V88, P1516
- (17) Qian, S; Cell Regul 1991, V2, P241 HCAPLUS
- (18) Sharma, H; J Cardiovasc Pharmacol 1992, V20(1), PS23
- (19) Shirakata, M; Genes Dev 1993, V7, P2456 HCAPLUS
- (20) Studier, F; Methods Enzymol 1990, V185, P60 HCAPLUS
- (21) Thompson, N; Growth Factors 1988, V1, P91 MEDLINE
- (22) Wu, C; Transplantation 1992, V54, P326 MEDLINE

L58 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:330462 HCAPLUS

DN 130:350322

TI Methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding

IN Lee, Se-Jin; McPherron, Alexandra C.

PA The Johns Hopkins University School of Medicine, USA

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12Q001-68

ICS C12P019-34; C07K016-00; C07H021-04

CC 13-6 (Mammalian Biochemistry)

Section cross-reference(s): 3, 17

FAN.CNT 7

| PATENT NO. | KIND  | DATE     | APPLICATION NO. | DATE         |
|------------|---|----------|-----------------|--------------|
| WO 9924618 | A1  | 19990520 | WO 1998-US23850 | 19981110 <-- |
| W:         | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, |          |                 |              |



MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,  
 TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9913909 A1 19990531 AU 1999-13909 19981110 <--

PRAI US 1997-967089 A 19971110 <--

WO 1998-US23850 W 19981110 <--

AB Methods for detecting allelic variants of the **myostatin** (growth and differentiation factor-8) gene are provided. Specifically provided are methods of identifying subjects having or having a predisposition for increased **muscle** mass as compared to subjects having wild-type **myostatin**. Increased **muscle** mass is particularly desirable in meat animals, including cattle, swine, sheep, poultry and fish. Two high **muscle** mass breeds of cattle, Piedmontese and Belgian Blue, had new alleles of the **myostatin** gene with **mutations** in exon 3. Cloning of the **myostatin** genes of humans and a no. of livestock animals is described. Primers and probes for the detection of wild-type and Belgian Blue and Piedmontese alleles of the cattle **myostatin** gene are described.

ST **muscle** mass livestock **myostatin** gene alleles;  
 Piedmontese cattle **muscle** mass **myostatin** variant;  
 Belgian Blue cattle **muscle** mass **myostatin** variant

IT Beef cattle  
 (Belgian Blue, **myostatin** gene of; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Beef cattle  
 (Piedmontese, **myostatin** gene of; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT **Mutation**  
 (deletion, in **myostatin** gene in high **muscle** mass cattle; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Nucleic acid hybridization  
 PCR (polymerase chain reaction)  
 RFLP (restriction fragment length polymorphism)  
 (for detection of alleles of **myostatin** gene; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Primers (nucleic acid)  
 Probes (nucleic acid)  
 RL: AGR (Agricultural use); ARG (Analytical reagent use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (for detection of alleles of **myostatin** gene; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Breeding, animal  
 (for lean **muscle** mass; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Test kits  
 (for screening for alleles of **myostatin** genes; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT Genetic polymorphism  
 (in **myostatin** genes; methods for detection of alleles of **myostatin** genes that affect lean **muscle** mass and their use in animal breeding)

IT **Muscle**  
 (methods for detection of alleles of **myostatin** genes that

affect lean **muscle** mass and their use in animal breeding)

IT Baboon  
 Chicken (Gallus domesticus)  
 Danio rerio  
 Mouse  
 Rat  
 Sheep  
 Swine  
 Turkey  
 (**myostatin** gene of; methods for detection of alleles of  
**myostatin** genes that affect lean **muscle** mass and  
 their use in animal breeding)

IT Gene, animal  
 RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL  
 (Biological study); USES (Uses)  
 (**myostatin**, alleles of in breeding livestock **muscle**  
 mass; methods for detection of alleles of **myostatin** genes  
 that affect lean **muscle** mass and their use in animal  
 breeding)

IT Growth factors, animal  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU  
 (Biological use, unclassified); FFD (Food or feed use); BIOL (Biological  
 study); PROC (Process); USES (Uses)  
 (**myostatins**; methods for detection of alleles of  
**myostatin** genes that affect lean **muscle** mass and  
 their use in animal breeding)

IT Alleles  
 (of **myostatin** genes; methods for detection of alleles of  
**myostatin** genes that affect lean **muscle** mass and  
 their use in animal breeding)

IT Mutation  
 (**transition**, in **myostatin** gene in high  
**muscle** mass cattle; methods for detection of alleles of  
**myostatin** genes that affect lean **muscle** mass and  
 their use in animal breeding)

IT 224952-91-4 224952-92-5  
 RL: AGR (Agricultural use); ARG (Analytical reagent use); PRP  
 (Properties); ANST (Analytical study); BIOL (Biological study); USES  
 (Uses)  
 (primer for detection of **myostatin** gene alleles; methods for  
 detection of alleles of **myostatin** genes that affect lean  
**muscle** mass and their use in animal breeding)

IT 224952-93-6 224952-94-7 224952-97-0 224953-00-8 224953-02-0  
 224953-04-2 224953-07-5 225105-45-3  
 RL: AGR (Agricultural use); ARG (Analytical reagent use); PRP  
 (Properties); ANST (Analytical study); BIOL (Biological study); USES  
 (Uses)  
 (probe for detection of **myostatin** gene alleles; methods for  
 detection of alleles of **myostatin** genes that affect lean  
**muscle** mass and their use in animal breeding)

IT 224952-95-8 224952-96-9  
 RL: AGR (Agricultural use); BUU (Biological use, unclassified); PRP  
 (Properties); BIOL (Biological study); USES (Uses)  
 (target for detection of alleles of cattle **myostatin** gene;  
 methods for detection of alleles of **myostatin** genes that  
 affect lean **muscle** mass and their use in animal breeding)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Dickman, S; Science 1997, V277, P1922 HCAPLUS  
 (2) Grobet; Nature Genetics 1997, V17, P71 HCAPLUS  
 (3) Kambadur; Genome Research 1997, V7, P910 HCAPLUS  
 (4) Research Genetics; Nucleic Acids Research 1994, V22(15)  
 (5) Vijg; US 5814491 A 1998 HCAPLUS

(6) Westhusin, M; Nature Genetics 1997, V17, P4 HCAPLUS

L58 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:64915 HCAPLUS

DN 130:134990

TI **Mutations** in the **myostatin** gene cause double-  
**muscling** in mammals

IN Grobet, Luc; Georges, Michel; Poncelet, Dominique

PA University of Liege, Belg.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-00

ICS C12N015-12; C07K014-495; C12N005-10; C12Q001-68; A01K067-027;  
A61K048-00

CC 3-3 (Biochemical Genetics)

Section cross-reference(s): 6, 13, 14, 63

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE         | APPLICATION NO. | DATE         |
|------|---|------|--------------|-----------------|--------------|
| PI   | WO 9902667  | A1   | 19990121     | WO 1998-IB1197  | 19980714 <-- |
|      | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |              |                 |              |
|      | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |              |                 |              |
|      | US 6103466  | A    | 20000815     | US 1997-891789  | 19970714 <-- |
|      | AU 9884571  | A1   | 19990208     | AU 1998-84571   | 19980714 <-- |
|      | EP 1002068  | A1   | 20000524     | EP 1998-935228  | 19980714 <-- |
|      | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |              |                 |              |
|      | JP 2001509378   | T2   | 20010724     | JP 2000-502165  | 19980714 <-- |
| PRAI | US 1997-891789  | A2   | 19970714 <-- |                 |              |
|      | US 1998-7761  | A2   | 19980115 <-- |                 |              |
|      | WO 1998-IB1197  | W    | 19980714 <-- |                 |              |

AB Genes (cDNA) encoding bovine and human **myostatin** proteins are provided contg. open reading frames encoding proteins of 375 amino acids in length. A mutant gene in which the coding sequence lacks an 11-bp consecutive sequence of the sequence encoding bovine protein having **myostatin** activity was sequenced. Cattle of the Belgian Blue breed homozygous for the mutant gene lacking **myostatin** activity are double-muscled. A method for detg. the presence of muscular hyperplasia in a mammal is described. The method includes obtaining a sample of material contg. DNA from the mammal and ascertaining whether a sequence of the DNA encoding (a) a protein having biol. activity of **myostatin**, is present, and whether a sequence of the DNA encoding (b) an allelic protein lacking the activity of (a), is present. The absence of (a) and the presence of (b) indicates the presence of muscular hyperplasia in the mammal.

ST **myostatin** gene sequence mutation muscular hyperplasia;  
bovine **myostatin** gene mutation muscular hyperplasia;  
human **myostatin** gene mutation muscular hyperplasia

IT PCR (polymerase chain reaction)  
(RT-PCR (reverse transcription-PCR), primers for diagnostic kit;  
mutations in the **myostatin** gene cause double-  
**muscling** in mammals)

IT cDNA sequences  
(for **myostatin** from bovine and human)

- IT Diagnosis  
(genetic; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT Ribozymes  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(increasing **muscle** mass by treatment with; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT **Muscle**, disease  
(muscular hyperplasia; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT Cattle  
Genetic mapping  
Molecular cloning  
**Mutation**  
Test kits  
(**mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(**mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT Primers (nucleic acid)  
Probes (nucleic acid)  
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(**mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT **Proteins**, specific or class  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(**myostatins**; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT **Protein** sequences  
(of **myostatin** from bovine and human)
- IT DNA sequences  
(of **myostatin** gene from bovine)
- IT Genetic mapping  
(phys.; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT 219991-75-0 219991-76-1  
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(PCR primer; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT 161135-86-0 219991-53-4, **Myostatin** (cattle)  
219991-78-3  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(amino acid sequence; **mutations** in the **myostatin** gene cause double-muscling in mammals)
- IT 219991-52-3, DNA (cattle **myostatin** cDNA plus flanks)  
219991-54-5, DNA (human **myostatin** cDNA plus flanks)  
219991-68-1, DNA (cattle **myostatin** gene plus flanks)  
219991-77-2  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; **mutations** in the **myostatin**

gene cause double-muscling in mammals)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Charlier; Mammalian Genome 1995, V6(11), P788 HCAPLUS
- (2) Dickman; Science 1997, V277(5334), P1922 HCAPLUS
- (3) Georges; Genome Research 1996, V6, P907 HCAPLUS
- (4) Grobet; Mamm Genome 1998, V9(3), P210 HCAPLUS
- (5) Grobet; Nature Genetics 1997, V17(1), P71 HCAPLUS
- (6) Kambadur; Genome Research 1997, V7(9), P910 HCAPLUS
- (7) Kappes; Genome Research 1997, V7, P235 HCAPLUS
- (8) McPherron; Nature 1997, V387, P83 HCAPLUS
- (9) McPherron; Proc Natl Acad Sci USA 1997, V94(23), P12457 HCAPLUS
- (10) Smith; Mammalian Genome 1997, V8(10), P742 HCAPLUS
- (11) Univ Johns Hopkins Med; WO 9421681 A 1994 HCAPLUS
- (12) Univ Johns Hopkins Med; WO 9833887 A 1998 HCAPLUS
- (13) Westhusin, M; Nature Genetics 1997, V17(1), P4 HCAPLUS
- (14) Westhusin, M; Nature Genetics 1997, V17(1), P71

L58 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:744046 HCAPLUS

DN 130:149113

TI **Myostatin mutations** cause double **muscling** in  
cattle

AU Smith, Timothy P.; Casas, Eduardo; Fahrenkrug, Scott C.; Stone, Roger T.;  
Kappes, Steven M.; Keele, John W.

CS USDA, ARS, U.S. Meat Animal Research Center, Clay Center, NE, 68933-0166,  
USA

SO Proceedings - Annual Reciprocal Meat Conference, American Meat Science  
Association (1998), 51st, 112-117  
CODEN: PRMCAC; ISSN: 0198-8999

PB National Live Stock and Meat Board

DT Journal; General Review

LA English

CC 3-0 (Biochemical Genetics)

Section cross-reference(s): 13

AB A review with 14 refs. on the identification of the double  
**muscling** gene as the gene for **myostatin** in cattle. The  
double **muscling** cattle breeds Belgian Blue and Asturiana contain  
a translational frameshift **mutation** in the 3rd exon of the  
**myostatin** gene MSTN. Double **muscled** Piedmont cattle  
contain a G.fwdarw.A transition **mutation** that changes a cysteine  
to a tyrosine. Further anal. of other double **muscled** breeds has  
identified 5 independent **mutations**, all of which are predicted  
to disrupt the function of the **protein**.

ST review **myostatin mutation** double **muscling**  
cattle

IT Gene, animal

RL: AGR (Agricultural use); BOC (Biological occurrence); BSU (Biological  
study, unclassified); PRP (Properties); BIOL (Biological study); OCCU  
(Occurrence); USES (Uses)

(MSTN; **myostatin mutations** cause double  
**muscling** in cattle)

IT Phenotypes

(double **muscling**; **myostatin mutations**  
cause double **muscling** in cattle)

IT Cattle

**Muscle**

**Mutation**

(**myostatin mutations** cause double **muscling**  
in cattle)

IT Growth factors, animal

RL: AGR (Agricultural use); BOC (Biological occurrence); BSU (Biological  
study, unclassified); PRP (Properties); BIOL (Biological study); OCCU

(Occurrence); USES (Uses)

(**myostatin**; **mutations** cause double **muscling**  
in cattle)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Arthur, P; Aust J Agric Res 1995, V46, P1493
- (2) Beever, J; Proc Plant and Animal Genome VI 1998, P32
- (3) Casas, E; J Anim Sci 1998, V76, P468 HCAPLUS
- (4) Charlier, C; Mamm Genome 1995, V6, P788 HCAPLUS
- (5) Chowdhary, B; Mamm Genome 1996, V7, P297 HCAPLUS
- (6) Dunner, S; Mamm Genome 1997, V8, P430 HCAPLUS
- (7) Fujii, J; Science 1991, V253, P448 HCAPLUS
- (8) Grobet, L; Mamm Genome 1998, V9, P210 HCAPLUS
- (9) Grobet, L; Nature Genet 1997, V17, P71 HCAPLUS
- (10) Kambadur, R; Genome Res 1997, V7, P910 HCAPLUS
- (11) McPherron, A; Proc Natl Acad Sci USA 1997, V94, P12457 HCAPLUS
- (12) Smith, T; Mamm Genome 1997, V8, P742 HCAPLUS
- (13) Solinas-Toldo, S; Genomics 1995, V27, P489 HCAPLUS
- (14) Sonstegard, T; Mamm Genome 1997, V8, P751 HCAPLUS

L58 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:177070 HCAPLUS

DN 128:279422

TI Molecular definition of an allelic series of **mutations**  
disrupting the **myostatin** function and causing double-  
**muscling** in cattle

AU Grobet, Luc; Poncelet, Dominique; Royo, Luis Jose; Brouwers, Benoit;  
Pirottin, Dimitri; Michaux, Charles; Menissier, Francois; Zanotti, Marta;  
Dunner, Susana; Georges, Michel

CS Dep. Genetics, Fac. Veterinary Med., Univ. Liege, Liege, 4000, Belg.

SO Mammalian Genome (1998), 9(3), 210-213

CODEN: MAMGEC; ISSN: 0938-8990

PB Springer-Verlag New York Inc.

DT Journal

LA English

CC 3-3 (Biochemical Genetics)

Section cross-reference(s): 6, 13

AB We have detd. the entire **myostatin** coding sequence for 32  
double-**muscled** cattle sampled from ten European cattle breeds.  
Seven DNA sequence polymorphisms were identified, of which five would be  
predicted to disrupt the function of the **protein**, one is a  
conservative amino acid **substitution**, and one a silent DNA  
sequence variant. Four **addnl.** DNA sequence polymorphisms were  
identified in **myostatin** intronic sequences. In all but two  
breeds, all double-**muscled** animals were either homozygous or  
compd. heterozygotes for one of the five loss-of-function  
**mutations**. The absence of obvious loss-of-function  
**mutations** in the coding sequence of the two remaining breeds  
points either towards **addnl. mutations** in unexplored  
segments of the gene, or towards locus heterogeneity of double-  
**muscling**.

ST **myostatin** gene mutation double **muscling**  
cattle

IT Phenotypes

(double-**muscling**; mol. definition of allelic series of  
**mutations** disrupting **myostatin** function and causing  
double-**muscling** in cattle)

IT **Mutation**

(loss-of-function; mol. definition of allelic series of  
**mutations** disrupting **myostatin** function and causing  
double-**muscling** in cattle)

IT Cattle

DNA sequences



Genetic polymorphism

**Protein sequences**

(mol. definition of allelic series of **mutations** disrupting **myostatin** function and causing double-**muscling** in cattle)

IT Growth factors, animal

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(**myostatin**; mol. definition of allelic series of **mutations** disrupting **myostatin** function and causing double-**muscling** in cattle)

L58 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:768637 HCAPLUS

DN 128:57742

TI Double **muscling** in cattle due to **mutations** in the **myostatin** gene

AU Mcpherron, Alexandra C.; Lee, Se-Jin

CS Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1997), 94(23), 12457-12461

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 2-10 (Mammalian Hormones)

Section cross-reference(s): 3, 12, 14

AB **Myostatin** (GDF-8) is a member of the transforming growth factor .beta. superfamily of secreted growth and differentiation factors that is essential for proper **regulation** of skeletal **muscle** mass in mice. Here the authors report the **myostatin** sequences of nine other vertebrate species and the identification of **mutations** in the coding sequence of bovine **myostatin** in two breeds of double-**muscled** cattle, Belgian Blue and Piedmontese, which are known to have an increase in **muscle** mass relative to conventional cattle. The Belgian Blue **myostatin** sequence contains an 11-nucleotide **deletion** in the third exon which causes a frameshift that eliminates virtually all of the mature, active region of the mol. The Piedmontese **myostatin** sequence contains a missense **mutation** in exon 3, resulting in a **substitution** of tyrosine for an invariant cysteine in the mature region of the **protein**. The similarity in pheno-types of double-**muscled** cattle and **myostatin** null mice suggests that **myostatin** performs the same biol. function in these two species and is a potentially useful target for genetic manipulation in other farm animals.

ST vertebrate DNA **protein** sequence **myostatin**; **muscling** cattle **myostatin** gene **mutation**

IT Cattle

(Belgian Blue and Piedmontese; double **muscling** in cattle due to **mutations** in **myostatin** gene)

IT Gene, animal

RL: PRP (Properties)

(MSTN; double **muscling** in cattle due to **mutations** in **myostatin** gene)

IT **Mutation**

(**deletion**; double **muscling** in cattle due to **mutations** in **myostatin** gene)

IT Cell differentiation

Chicken (*Gallus domesticus*)

Danio rerio

Papio hamadryas

**Protein sequences**Rat (*Rattus norvegicus*)

Sheep

Swine

Turkey

Vertebrate (Vertebrata)

**cDNA sequences**(double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Muscle**(doubling; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Mutation**(frameshift; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Protein sequences**(homol.; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Evolution**(mol.; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Growth factors, animal**

RL: PRP (Properties)

(myostatins; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Mutation**(nonsense; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Mutation**(substitution; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Mutation**(transition; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **Transforming growth factors**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(.beta.-; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **161135-86-0, Growth/differentiation****factor 8 (human) 199810-41-8****199810-42-9, Myostatin (cattle muscle gene****MSTN) 199810-43-0, Myostatin (chicken muscle****gene MSTN) 199810-44-1, Myostatin (sheep****muscle gene MSTN) 199810-45-2, Myostatin****(swine muscle gene MSTN) 199810-46-3****199810-47-4, Myostatin (turkey muscle gene****MSTN) 199810-48-5, Myostatin (Danio rerio****muscle gene MSTN)**

RL: PRP (Properties)

(amino acid sequence; double **muscling** in cattle due to **mutations** in **myostatin** gene)IT **200048-13-1, GenBank AF019619 200048-14-2, GenBank****AF019620 200048-15-3, GenBank AF019621 200048-16-4,****GenBank AF019622 200048-17-5, GenBank AF019623****200048-18-6, GenBank AF019624 200048-19-7, GenBank****AF019625 200048-20-0, GenBank AF019626 200048-21-1,****GenBank AF019627**

RL: PRP (Properties)

(nucleotide sequence; double **muscling** in cattle due to **mutations** in **myostatin** gene)

L58 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:600692 HCAPLUS

DN 127:315882

TI **Mutations in myostatin (GDF8) in double-muscled Belgian Blue and Piedmontese cattle**

AU Kambadur, Ravi; Sharma, Mridula; Smith, Timothy P. L.; Bass, John J.

CS AgResearch, Hamilton, N. Z.

SO Genome Research (1997), 7(9), 910-916  
CODEN: GEREFS; ISSN: 1088-9051

PB Cold Spring Harbor Laboratory Press

DT Journal

LA English

CC 6-3 (General Biochemistry)  
Section cross-reference(s): 3, 13, 14

AB A visibly distinct muscular hypertrophy (mh), commonly known as double **muscling**, occurs with high frequency in the Belgian Blue and Piedmontese cattle breeds. The autosomal recessive mh locus causing double-**muscling** condition in these cattle maps to bovine chromosome 2 within the same interval as **myostatin**, a member of the TGF- $\beta$  superfamily of genes. Because targeted disruption of **myostatin** in mice results in a muscular phenotype very similar to that seen in double-**muscled** cattle, we have evaluated this gene as a candidate gene for double-**muscling** condition by cloning the bovine **myostatin** cDNA and examg. the expression pattern and sequence of the gene in normal and double-**muscled** cattle. The anal. demonstrates that the levels and timing of expression do not appear to differ between Belgian Blue and normal animals, as both classes show expression initiating during fetal development and being maintained in adult **muscle**. Moreover, sequence anal. reveals **mutations** in heavy-**muscled** cattle of both breeds. Belgian Blue cattle are homozygous for an 11-bp **deletion** in the coding region that is not detected in cDNA of any normal animals examd. This **deletion** results in a frame-shift **mutation** that removes the portion of the **Myostatin protein** that is most highly conserved among TGF- $\beta$  family members and that is the portion targeted for disruption in the mouse study. Piedmontese animals tested have a G-A transition in the same region that changes a cysteine residue to a tyrosine. This **mutation** alters one of the residues that are hallmarks of the TGF- $\beta$  family and are highly conserved during evolution and among members of the gene family. It therefore appears likely that the mh allele in these breeds involves **mutation** within the **myostatin** gene and that **myostatin** is a neg. **regulator** of **muscle** growth in cattle as well as mice.

ST cattle cDNA sequence **myostatin** GDF8; **protein** sequence  
cattle **myostatin** GDF8; developmental expression  
**myostatin** gene GDF8 cattle

IT **Protein** sequences  
cDNA sequences  
(cloning and sequencing of bovine **myostatin**)

IT **Mutation**  
(**deletion**; 11-bp **deletion** in the **myostatin** (GDF8) gene in Belgian Blue cattle results in a frame-shift **mutation** in the **myostatin** protein)

IT Embryo, animal  
**Muscle**  
(developmental expression of the bovine **myostatin** (GDF8) gene in normal and double-**muscled** Belgian Blue cattle and expression in different adult **muscles**)

IT Gene  
(expression; developmental expression of the bovine **myostatin** (GDF8) gene in normal and double-**muscled** Belgian Blue cattle and expression in different adult **muscles**)

IT Embryo, animal  
(fetus; developmental expression of the bovine **myostatin**

- (GDF8) gene in normal and double-muscled Belgian Blue cattle and expression in different adult muscles)
- IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(for myostatin (GDF8); cloning and sequencing of bovine myostatin)
- IT Muscle, disease  
(hypertrophy; mutations in myostatin (GDF8) gene in double-muscled Belgian Blue and Piedmontese cattle)
- IT Cattle  
(mutations in myostatin (GDF8) gene in double-muscled Belgian Blue and Piedmontese cattle)
- IT Proteins, specific or class  
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)  
(myostatin; cloning and sequencing of bovine myostatin)
- IT Mutation  
(transition; transition mutation  
(G.fwdarw.A) found in the myostatin (GDF8) gene in Piedmontese cattle)
- IT 197731-05-8, Myostatin (cattle reduced)  
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)  
(amino acid sequence; cloning and sequencing of bovine myostatin)
- IT 197431-01-9, DNA (cattle myostatin cDNA)  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(nucleotide sequence; cloning and sequencing of bovine myostatin)